EXHIBIT A

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Contributing Factors Associated with Prescription Opioid Supply and Opioid Attributable Costs in Montgomery County, Ohio

Expert Report of John E. Schneider, PhD

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1. INTRODUCTION

1.1. The principal objectives of this report are as follows: (1) provide background on opioid use in the U.S. and the contributing factors associated with opioid supply, use and misuse; (2) provide an analysis of opioid misuse in the context of the economic treatment of "externalities;" (3) identify and discuss responsible parties associated with the externality; (4) provide an analysis of implications for Montgomery County, Ohio; (5) provide a critical analysis of the expert reports submitted by David Cutler and Caleb Alexander in the Montgomery County matter.

1.2. The main sources of information and data relied upon for this analysis are publicly available data, reports, and peer-reviewed literature, all of which are cited in footnotes throughout the report and summarized in a bibliography at the end. Many of the materials cited in my report rely on multiple methods and contain multiple findings; in some cases, these materials also contain summary opinions by the authors. In my citing of published studies, data sources, or reports, I am *not* implicitly or explicitly supporting, endorsing or agreeing with all the data, findings, and opinions contained in the citation. The facts and opinions expressed in this report represent at this time my opinions related to contributing factors and liability. However, I reserve the right to modify, expand, or edit this report if any new information or data (i.e., newly disclosed, newly published, or newly released) becomes available after the report date indicated above.

1.3. My opinions and conclusions are all within a reasonable degree of certainty in the field of health economics, the field in which I have been materially involved my entire professional career. The methods employed in this analysis are reasonable and rational and would be considered so by peers in the field of health economics. I base this on my active participation in the field of health economics for the past 30 years. In addition to earning a PhD in Health Economics at the University of California, Berkeley, in 2000, my experiences have included several professional appointments, including: Research Analyst at the Center for Health Economics Research (1989-1993), Research Assistant at the University of California, Berkeley, School of Public Health (1994-1999); Director of Research at the California Association of Health Plans (1999-2001); Assistant Professor at the University of Iowa, Department of Health Management & Policy and Department of Economics (2001-2008); and Senior Director with the international health economics consultancy Oxford Outcomes Ltd., a division of ICON plc (2009-2013). While at the University of Iowa, I was the recipient of a prestigious three-year Merit Award from Veterans Health Administration.

1.4. In addition to being a Principal and Health Economist with Avalon Health Economics (Morristown NJ; Miami, FL; London, UK), I have also been part of a multi-year grant to Columbia University to study gene variant reinterpretation and a multi-year contract with the State of California (through San Diego State University) to study the attributable environmental cost of tobacco. I also have more than 54 peer-reviewed publications in the field of health economics, including journal articles, book sections, and one book. I have

skills and expertise in economics, health economics, health services and policy analysis, public health, epidemiology, and biostatistics. For more detail, see attached CV.

1.5. Some of the work that I have done throughout my career has focused on economics of externalities and attributable abatement costs. Examples of these include: (1) studies of the externalities associated with tobacco outlet density, and its impact on smoking prevalence; (2) studies of the environmental externalities associated with tobacco production and use, via research grants and contracts with the World Health Organization ("WHO"), the City of San Francisco, and San Diego State University (where I participate in an interdisciplinary team focused on the attributable costs and abatement costs associated with environmental impact of tobacco use in the state of California); (3) a study of the attributable costs of calorically sweetened beverages ("CSBs") for the City of San Francisco; (4) a study of the environmental impact of tobacco product litter ("TPW") for the City of San Francisco; and (5) a study of the attributable costs of alcohol misuse for the City of San Francisco. For most of these engagements, it was critical to (a) gain an in-depth understanding of how state and local governments manage externalities associated with pollution, tobacco use, substance abuse, and poor diet (i.e., the attributable costs of the externalities), and (b) identify the parties responsible for the externalities. In addition, I have provided expert testimony in a wide variety of research projects and cases involving the calculation of attributable economic damages, including the use of statistical methods to determine costs attributable to various health and environmental factors.

1.6. I have worked independently on this research and report. However, for some general background research I had the support from some of the full-time staff from Avalon Health Economics ("AHE"), where I am a full-time salaried employee and Principal. A salaried employee, I received no additional compensation directly associated with conducting this research. The rates charged by AHE for this research are $400 per hour for my time and $250 per hour for staff support.

1.7. Following this brief introduction, this report is organized in six sections, each of which aligns with the report objectives identified above: (1) background on opioid use in the U.S. and the contributing factors associated with opioid supply, use and misuse; (2) analysis of opioid misuse in the context of the economic treatment of "externalities;" (3) identification of responsible parties associated with the externality; and (4) analysis and discussion of implications for Montgomery County, Ohio; (5) critique and analysis of the expert reports submitted by David Cutler and Caleb Alexander.

2. BACKGROUND

2.1. *Definitions*. Opioids refer generally to a class of prescription drugs that include pain relievers such as oxycodone (OxyContin®), hydrocodone (Vicodin®), codeine, morphine, and others, all of which have been approved by the U.S. Food and Drug Administration ("FDA").[1] In addition to opioids available legally by prescription, there are also illegal

[1] FDA, "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," (U.S. Food and Drug Administration, 2021).

"street" versions of opioids, such as heroin and synthetic fentanyl.[2] In this report, I use the term "opioids" to refer generally to this class of drugs. When discussing the "misuse" of opioids, in some instances this may also include illegal compounds such as heroin, depending on the source data in question and the context.

2.2. *History*. It is important to understand how opioid use in the U.S. evolved from a pharmacological pain treatment to a public health concern.[3] Medical and non-medical use of opioids globally has a long history and is believed to date as far back as the sixteenth century.[4] In the intervening decades, a combination of economic cycles, conflicts, wars, and other factors have resulted in periods of fluctuation in the use and misuse of opioids throughout many different parts of the world.[5] In the U.S., the most recent change in opioid use and misuse began roughly 30 years ago, in the early 1990s, following the FDA approval of the first long-acting (12-hour) opioid-based pain relievers MS Contin (1987) and OxyContin (1995),[6] and in parallel with an shift in the healthcare sector toward patient-centered care and emphasis on pain management as the "fifth vital sign."

2.3. *Non-Medical Use*. The term "non-medical" use of opioids typically refers to an instance of opioid use that is inconsistent with how the medication was prescribed by a medical care provider.[7] The non-medical use of opioids is broadly defined, including prescription drug "non-adherence" (e.g., taking medications at intervals different than prescribed),[8] but also including behaviors that could be considered "misuse." The term "opioid use disorder" ("OUD"), which is listed in the American Psychiatric Association DSM-5, generally refers to repeated or consistent misuse of opioids, and includes more serious forms of abuse or addiction.[9] Thus, misuse is a subset of non-medical use, and OUD is a

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[2] According to the National Institute on Drug Abuse (NIDA), heroin is defined as "an opioid drug made from morphine, a natural substance taken from the seed pod of the various opium poppy plants grown in Southeast and Southwest Asia, Mexico, and Colombia. Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin." See NIDA, "Heroin Drug Facts," (Washington, D.C.: National Institute on Drug Abuse | U.S. National Institutes for Health, 2021).

[3] See generally H. Joseph, S. Stancliff, and J. Langrod, "Methadone maintenance treatment (MMT): a review of historical and clinical issues," *Mt Sinai J Med* 67, no. 5-6 (2000); R. G. Lande, "American Civil War medical practice, the post-bellum opium crisis and modern comparisons," *Hist Psychiatry* 31, no. 4 (2020).

[4] A. Moosavyzadeh et al., "The medieval Persian manuscript of Afyunieh: the first individual treatise on the opium and addiction in history," *J Integr Med* 16, no. 2 (2018).

[5] A. Case and A. Deaton, *Deaths of Despair and the Future of Capitalism* (Princeton, NJ: Princeton University Press, 2020).

[6] FDA, "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse."

[7] J. M. Tetrault and J. L. Butner, "Non-Medical Prescription Opioid Use and Prescription Opioid Use Disorder: A Review," *Yale J Biol Med* 88, no. 3 (2015); E. Ulker and E. Del Fabbro, "Best Practices in the Management of Nonmedical Opioid Use in Patients with Cancer-Related Pain," *Oncologist* 25, no. 3 (2020).

[8] For background refer to R. Nieuwlaat et al., "Interventions for enhancing medication adherence," *Cochrane Database Syst Rev* 2014, no. 11 (2014).

[9] See generally A. M. Dydyk, N. K. Jain, and M. Gupta, "Opioid Use Disorder," in *StatPearls* (Treasure Island (FL): StatPearls Publishing LLC., 2021).

subset of misuse. Hereafter, consistent with the literature, I use the term OUD to similarly refer to serious abuse or addiction. According to the National Survey on Drug Use and Health ("NSDUH"), which is based on a sample of the U.S. population ages 18 and older, the current prevalence of "prescription pain reliever use disorder" in the past year was 0.89%.[10] In addition to OUD, misuse of opioids during pregnancy can in some cases be associated with neonatal abstinence syndrome ("NAS")[11] and neonatal opioid withdrawal syndrome ("NOWS").

2.4. *Prescription Opioids*. In this report, my focus is on the supply of *prescription* opioids, as plaintiffs in cases involving retail pharmacies suggest that (to some alleged extent) the supply of opioids, which consists of prescription opioids and illicit opioids, is in some way related to the prevalence of OUD. There are two common ways of measuring prescription opioids: number of prescriptions dispensed, or morphine milligram equivalents ("MME"), which accounts variation in dosage. Both measures are commonly featured in opioid studies, with many studies reporting outcomes based on both. In this report, I focus on the number of prescriptions rather than MMEs, for three reasons. First, the "transaction" at issue in cases involving retail pharmacies is the legal dispensing of a dosage-specific prescription written by a licensed provider; that is, a retail pharmacy is dispensing a *prescription*, not a multiple of MMEs. Second, for clinical studies of the exact relationship between dosage and clinical outcome, MMEs may serve as a more appropriate measure. However, for studies of liability, costs, and policy, the legal unit of transaction (i.e., prescriptions) is more relevant. Third, several studies have shown that the two measures do not vary temporally (i.e., the levels move more or less in sync over time), and generally can substitute for one another in studies of prescribing patterns.[12]

2.5. From the late 1990s until around 2012, opioid prescription rates in the U.S. increased.[13] However, beginning in 2012, the total number of opioid prescriptions nationwide began to steadily fall, and continued to fall through 2020, which was the most recent year of data available at the time of this writing (Figure 2-1). The red dashed line in Figure 2-1 shows a plot of a two-year moving average.

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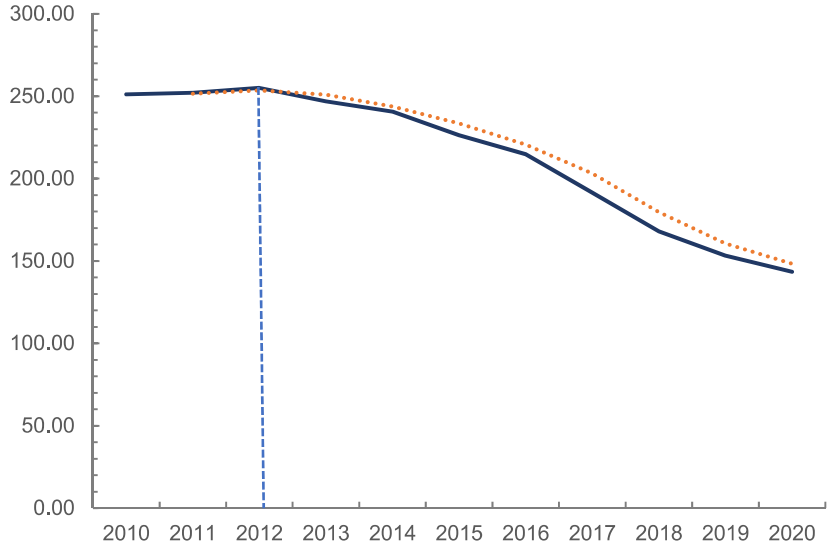
[10] The NSDUH defines "prescription pain reliever use disorder" as follows: "Prescription Pain Reliever Use Disorder (PRUD) data in 2020 are based on criteria from the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5)" Refer to "2018-2019 NSDUH State Estimates of Substance Use and Mental Disorders" (SAMHSA).

[11] Although NAS is often attributed to opioids, the definition of NAS refers generally to substance abuse during pregnancy, and the extent to which it can be attributed to opioids is unclear. See generally P. Kocherlakota, "Neonatal abstinence syndrome," *Pediatrics* 134, no. 2 (2014).

[12] For example, see M. V. Kiang et al., "Opioid prescribing patterns among medical providers in the United States, 2003-17: retrospective, observational study," *Bmj* 368 (2020); B. R. Meisenberg et al., "Assessment of Opioid Prescribing Practices Before and After Implementation of a Health System Intervention to Reduce Opioid Overprescribing," *JAMA Netw Open* 1, no. 5 (2018).

[13] CDC, "Opioid Precribing Data, 2006-2020," (Based on IQVIA Xponent data, 2006–2020; reported by U.S. Centers for Disease Control and Prevention 2022).

Figure 2-1. Total U.S. Opioid Prescriptions, 2010-2020
(millions)



2.6. The decline in opioid prescriptions was precipitated primarily by two factors: (1) response to changes in pain-related and opioid-specific clinical practice guidelines ("CPGs") on the part of physicians, medical societies and the Centers for Disease Control and Prevention ("CDC"), which (after considerable delay) cautioned providers as to the clinical tradeoffs associated with opioid use and emphasized caution in prescribing opioids;[14] and (2) increased state and federal government oversight and monitoring of opioid prescriptions [e.g., via prescription drug monitoring programs ("PDMPs")].[15] These two factors together generally led to higher levels of overall awareness and vigilance among clinicians, which in turn resulted in markedly and consistently declining prescription opioid utilization over the past decade.

2.7. *Contributing Factors*. Experts in the fields of medicine, public health, health policy and heath economics agree that "causation" of the supply of prescription opioids is

[14] There were many such guidelines issued by various medical societies and interest groups, but guidelines by the Centers for Disease Control and Prevention (CDC) summarized such guidelines. Refer to A. S. B. Bohnert, G. P. Guy, Jr., and J. L. Losby, "Opioid Prescribing in the United States Before and After the Centers for Disease Control and Prevention's 2016 Opioid Guideline," *Ann Intern Med* 169, no. 6 (2018); J. E. Goldstick et al., "Changes in Initial Opioid Prescribing Practices After the 2016 Release of the CDC Guideline for Prescribing Opioids for Chronic Pain," *JAMA Netw Open* 4, no. 7 (2021); L. Gumidyala et al., "Effect of CDC Opioid-Prescribing Guidelines in a Community Hospital Emergency Department," *J Public Health Manag Pract* 27, no. Suppl 3 (2021); J. F. Scherrer et al., "Comparison of Opioids Prescribed for Patients at Risk for Opioid Misuse Before and After Publication of the Centers for Disease Control and Prevention's Opioid Prescribing Guidelines," *JAMA Netw Open* 3, no. 12 (2020).

[15] For example, refer to R. S. D'Souza, M. Lang, and J. S. Eldrige, "Prescription Drug Monitoring Program," in *StatPearls* (Treasure Island (FL): StatPearls Publishing LLC, 2022); C. S. Davis, M. Pierce, and N. Dasgupta, "Evolution and convergence of state laws governing controlled substance prescription monitoring programs, 1998-2011," *Am J Public Health* 104, no. 8 (2014).

multifactorial.[16] From an economic perspective, these drivers can be ones that increase the supply of opioids or increase the demand for opioids. Indeed, the rise in opioid utilization, beginning in the mid to late 1990s, is attributed to several contributing factors, representing a mix of "supply push" and "demand-pull" factors. These contributing factors can also be thought of as "enabling" or "causative" factors, the influence of which combined in a synergistic and additive way to increase the volume of opioids on the market. Contributing causative factors are those that in some way created, enabled, perpetuated, or promoted opioid sales, either in the form of supply-push or demand-pull. The following factors have been identified by experts as critical causative drivers of the supply of prescription opioids: (1) regulatory approval; (2) changes in medical need; (3) government advocacy for pain management; (4) medical advocacy for pain management; (5) increased reliance on "quality" ratings in accreditation and reimbursement systems; (6) manufacturer marketing to physicians; and (7) macroeconomic factors (Figure 2-2).

[16] See generally S. A. Bernard et al., "Management of Pain in the United States-A Brief History and Implications for the Opioid Epidemic," *Health Serv Insights* 11 (2018); D. J. Clark and M. A. Schumacher, "America's Opioid Epidemic: Supply and Demand Considerations," *Anesth Analg* 125, no. 5 (2017); S. R. Friedman et al., "The Opioid/Overdose Crisis as a Dialectics of Pain, Despair, and One-Sided Struggle," *Front Public Health* 8 (2020); L. Manchikanti et al., "Opioid epidemic in the United States," *Pain Physician* 15, no. 3 Suppl (2012); W. M. Compton and C. M. Jones, "Epidemiology of the U.S. opioid crisis: the importance of the vector," *Ann N Y Acad Sci* 1451, no. 1 (2019); L. Manchikanti et al., "Reframing the Prevention Strategies of the Opioid Crisis: Focusing on Prescription Opioids, Fentanyl, and Heroin Epidemic," *Pain Physician* 21, no. 4 (2018).

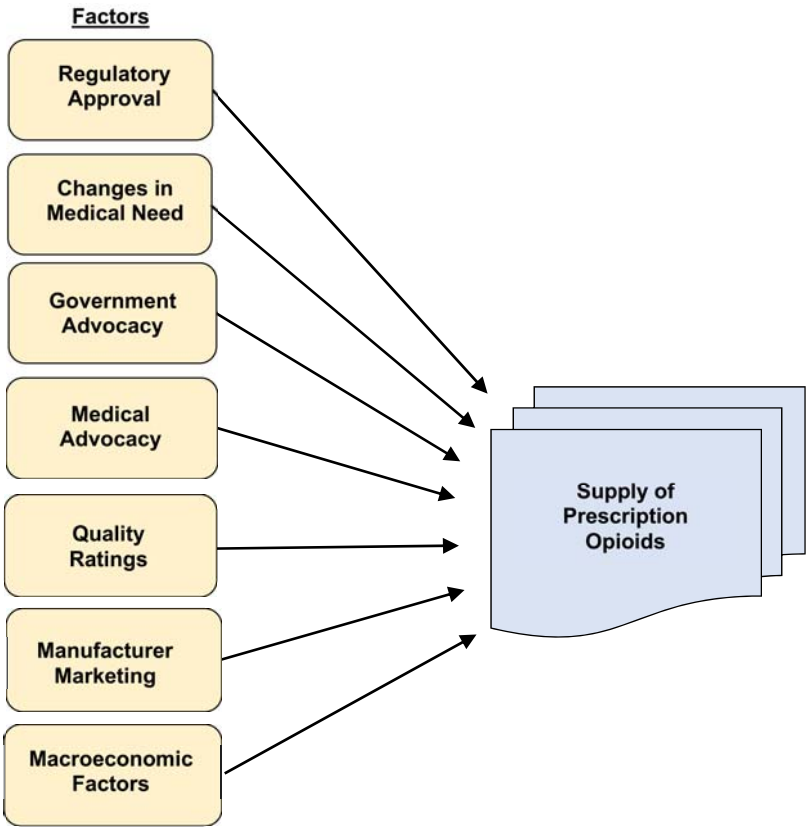


Figure 2-2. Contributing Factors Associated with Prescription Opioid Supply
Notes: See text.

2.8. *Regulatory Approval*. Approval by the primary regulator of prescription drugs in the U.S. is not only legally required before prescription drugs can be sold, but the "stamp of approval" conferred by FDA approval also directly and indirectly boosts drug sales.[17] In the U.S., prescription drugs must undergo rigorous clinical testing prior to entering the market. Clinical studies generally occur in three phases, and the investigational drug or device must successfully complete each phase. Only about 10% of investigational drugs survive from initial trial phases to final FDA approval.[18] The average cost of advancing a pharmaceutical compound through this process, ending in FDA approval, is more than $900 million per compound.[19] Clinical studies are typically carried out by manufacturers,

[17] See generally S.S. Mehta, *Commercializing Successful Biomedical Technologies: Basic Principles for the Development of Drugs, Diagnostics and Devices* (Cambridge, UK: Cambridge University Press, 2008).
[18] O. J. Wouters, M. McKee, and J. Luyten, "Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018," *Jama* 323, no. 9 (2020).
[19] See generally J. A. DiMasi, H. G. Grabowski, and R. W. Hansen, "Innovation in the pharmaceutical industry: New estimates of R&D costs," *J Health Econ* 47 (2016); Wouters, McKee, and Luyten,

but it is the FDA that evaluates the design and outcomes of these clinical studies as part of the regulatory approval process. Once a manufacturer submits its dossier of clinical evidence, the FDA conducts a rigorous assessment of the data, which typically takes about 12-18 months.[20] FDA approval is necessary before any prescription drug can be marketed or sold, and at launch newly approved drugs typically have a period of market exclusivity, depending on the age of associated patents. Thus, the combination of FDA approval and market exclusivity create powerful incentives for drug manufacturers to maximize sales in the window immediately after approval and prior to patent expiry.[21] During this window, the FDA is responsible for post-market surveillance and monitoring.[22]

2.9. As mentioned above, the FDA approved the first long-acting opioid-based pain relievers MS Contin in 1987 and OxyContin in 1995,[23] and approved fentanyl (Actiq) in 1998. It was not until 2001 (i.e., 14 years after the first opioid was approved) that the FDA began having meetings regarding the risks of prescription opioids. Apart from requiring changes in labeling, the first significant action taken by the FDA was a warning letter issued to a manufacturer in 2003, after long-acting opioids had been on the market for 16 years. Some experts have argued that FDA was negligent in both the approval process and in post-market surveillance. According to a recent article published in the *Journal of the American Medical Association*, entitled "How FDA Failures Contributed to the Opioid Crisis," "…despite this mounting criticism, FDA policies for approving and labeling opioids remain largely unchanged. The FDA has not undertaken a root cause analysis of its regulatory errors [and] to the contrary, the agency has adopted a defensive posture and sought to shift blame."[24]

2.10. *Changes in Medical Need*. It is important to note that the primary role of prescription opioids, and the basis for FDA approval of opioids, is clinical utility; that is, the clinical need to address patient pain. While clinical utility is normally expected to drive demand for applicable treatments, in the case of opioids, the timing of two important factors created an important added dimension that magnified medical need. First, increased life expectancy and improved survival rates from cancer and other chronic diseases added further demands on the health system to develop more effective means of controlling acute

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"Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018."

[20] See generally M. K. Keng, C. M. Wenzell, and M. A. Sekeres, "A drug's life: the pathway to drug approval," *Clin Adv Hematol Oncol* 11, no. 10 (2013); S. W. Moore, "An overview of drug development in the United States and current challenges," *South Med J* 96, no. 12 (2003).

[21] See generally A. Dabrowska and S. Thaul, "How FDA Approves Drugs and Regulates Their Safety and Effectiveness," (Washington, D.C.: Congressional Research Service, 2018); H. Grabowski et al., "Continuing trends in U.S. brand-name and generic drug competition," *J Med Econ* 24, no. 1 (2021); A. S. Kesselheim, J. Avorn, and A. Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform," *Jama* 316, no. 8 (2016).

[22] P. J. Pitts et al., "21st century pharmacovigilance: efforts, roles, and responsibilities," *Lancet Oncol* 17, no. 11 (2016).

[23] FDA, "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse."

[24] A. Kolodny, "How FDA Failures Contributed to the Opioid Crisis," *AMA J Ethics* 22, no. 1 (2020).

and chronic pain to a growing number of patients.[25] Second, FDA approval of opioids coincided with a major migration of care to outpatient and ambulatory surgery settings, especially for less invasive surgical procedures.[26] Outpatient settings require the discharge of patients within 24 hours and typically before pain subsides, thereby increasing the need for post-operative prescription analgesics.[27] Opioid-based pain management helped meet this rising demand, even if a substantial proportion of physician opioid prescribing at discharge was subsequently found to be inappropriate or excessive.[28]

2.11. *Government Advocacy*. Beginning in the late 1990s, there began an orchestrated effort throughout the U.S. public and private health care system to improve "patient centered" care generally and pain management specifically. Federal and state governments played a prominent and vocal role in the promotion of more aggressive pain management as part of patient-centered care and, more generally, "quality improvement." For example, in 2000, the U.S. Congress declared the beginning of a "Decade of Pain Control and Research."[29] A year later, the U.S. Institute of Medicine ("IOM") released its landmark study entitled *Crossing the Quality Chasm: A New Health System for the 21st Century*, in which the authors identified patient-centered care as one of the six primary domains of health care quality, defining it as "providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions."[30] A few years later the IOM released a more focused report devoted entirely to pain control as a means of addressing patient preferences and values.[31] During this time, a large number of campaigns explicitly advocated for improvement in pain control, regularly referring to pain as the "the fifth vital sign."[32] This messaging was

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[25] See generally V. Jairam et al., "National Patterns in Prescription Opioid Use and Misuse Among Cancer Survivors in the United States," *JAMA Network Open* 3, no. 8 (2020); A. Zajacova, H. Grol-Prokopczyk, and Z. Zimmer, "Pain Trends Among American Adults, 2002–2018: Patterns, Disparities, and Correlates," *Demography* 58, no. 2 (2021).

[26] See, for example, N. Mehta et al., "Trends in outpatient versus inpatient total shoulder arthroplasty over time," *JSES International* 6, no. 1 (2022).

[27] See generally K. Rajput and N. Vadivelu, "Acute Pain Management of Chronic Pain Patients in Ambulatory Surgery Centers," *Curr Pain Headache Rep* 25, no. 1 (2021); N. Rawal, "Postoperative pain treatment for ambulatory surgery," *Best Pract Res Clin Anaesthesiol* 21, no. 1 (2007); S. A. Schug and C. Chong, "Pain management after ambulatory surgery," *Curr Opin Anaesthesiol* 22, no. 6 (2009); C. L. Chen et al., "Long-Term Trends in Postoperative Opioid Prescribing, 1994 to 2014," *J Am Acad Orthop Surg Glob Res Rev* 4, no. 1 (2020).

[28] M. D. Neuman, B. T. Bateman, and H. Wunsch, "Inappropriate opioid prescription after surgery," *Lancet* 393, no. 10180 (2019).

[29] Refer to F. Brennan, "The US Congressional "Decade on Pain Control and Research" 2001-2011: A Review," *J Pain Palliat Care Pharmacother* 29, no. 3 (2015).

[30] IOM, *Crossing the Quality Chasm: A New Health System for the 21st Century* (Washington, D.C.: Institute of Medicine (IOM); National Academy Press, 2001).

[31] "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research," (U.S. National Institutes for Health | Institute of Medicine 2011).

[32] See generally N. Levy, J. Sturgess, and P. Mills, ""Pain as the fifth vital sign" and dependence on the "numerical pain scale" is being abandoned in the US: Why?," *Br J Anaesth* 120, no. 3 (2018); N. E. Morone and D. K. Weiner, "Pain as the fifth vital sign: exposing the vital need for pain education," *Clin Ther* 35, no. 11 (2013).

delivered frequently and consistently from virtually all government-based health care agencies associated with research, coverage, and reimbursement, including public payers like state Medicaid programs.[33]

2.12. *Medical Advocacy*. Partly in response to these large-scale health policy initiatives on the part of federal and state governments, beginning in the 1990s medical societies and medical research organizations began drafting policies, clinical pathways, and CPGs outlining processes, procedures, and "best practices" focused on improvement in diagnosis and treatment of various forms of acute and chronic pain. Examples of these activities are numerous and widespread.[34] A large number of medical societies actively promoted aggressive pain management and opioid utilization, including the U.S. Pain Foundation, the American Academy of Pain Medicine, the Academy of Integrated Pain Management, the American Pain Society, the National Pain Foundation, the American Chronic Pain Association, the American Society of Pain Management Nursing, the American Society of Pain Educators, the American Pain Foundation, and others.[35] While there was general awareness among the medical community and provider groups of the risks of opioids at this time,[36] the initial wave of clinical pain guidelines focused more on the aforementioned patient-centered care and the clinical effectiveness of pain control rather than on the risks and clinical tradeoffs associated with opioid-based pain medications. It is also important to note that many of the medical societies encouraging the use of prescription opioids for pain management also received funding from opioid manufacturers, and it is unclear the extent to which such funding may have influenced their medical policies.[37] Of the approximately 12 different medical societies promoting aggressive pain control, only 7 of them remain in existence.[38]

2.13. *Quality Ratings*. During the "Decade of Pain Control," but not necessarily directly a result of it, public and private payers began moving toward "value-based reimbursement" ("VBR") mechanisms which were generally structured to financially reward providers for

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[33] A useful overview of these efforts is available in S. Imhof and B. Kaskie, "How can we make the pain go away? Public policies to manage pain at the end of life," *Gerontologist* 48, no. 4 (2008).

[34] See generally APSQCC, "Quality improvement guidelines for the treatment of acute pain and cancer pain. American Pain Society Quality of Care Committee," *Jama* 274, no. 23 (1995); D. V. Ernstzen, Q. A. Louw, and S. L. Hillier, "Clinical practice guidelines for the management of chronic musculoskeletal pain in primary healthcare: a systematic review," *Implement Sci* 12, no. 1 (2017); K. L. Schmidt, M. A. Alpen, and B. A. Rakel, "Implementation of the Agency for Health Care Policy and Research Pain Guidelines," *AACN Clin Issues* 7, no. 3 (1996). For a list of medical societies prominently involved in the promotion of aggressive pain management, also see Manchikanti et al., "Reframing the Prevention Strategies of the Opioid Crisis: Focusing on Prescription Opioids, Fentanyl, and Heroin Epidemic."

[35] See, for example, Manchikanti et al.

[36] For example, based on a PubMed search with key words "opioid" and "misuse," between 1990 and 2000 there were between 400 and 500 publications per year containing both search terms.

[37] See generally Manchikanti et al.

[38] Using the list provided by Manchikanti et al. (Figure 7 in the paper), I investigated each of the 12 organizations listed, and determined that the following appear to be no longer in existence (with month and year ceased operations in parentheses): Academy of Integrative Pain Management (January 2019), American Pain Society (June 2019), American Pain Foundation (May 2012), American Society of Pain Educators (appears to have merged with another organization), and The National Pain Foundation (2010).

achieving higher scores on a variety of standardized assessments of quality of care. Examples of such measures are the Hospital Consumer Assessment of Healthcare Providers and Systems ("HCAHPS"), Merit-Based Incentive Payments ("MIPS"), and the Physician Quality Reporting System ("PQRS"). Each of these quality assessment tools includes one or more metrics directly and explicitly related to the effectiveness of pain management. Following implementation, studies showed (very consistently) that pain management was highly correlated with overall patient satisfaction;[39] thus, following the rapid diffusion of VBR-type reimbursement mechanisms, healthcare providers faced significant financial incentives to assure that patient pain was sufficiently managed. Opioid-based pain treatments were considered a cost-effective means of achieving pain management in a wide variety of applications,[40] and were embraced by clinicians, health systems, and payers as means of more readily achieving VBR goals.

2.14. Similarly, highly influential healthcare accreditation agencies joined the call for improvement in pain management by tying pain management to accreditation. For example, in 2001, the leading healthcare provider accreditation group "The Joint Commission" (formerly The Joint Commission on the Accreditation of Healthcare Organizations, or "JCAHO") drafted standards for organizations to improve pain management, "as part of a national effort to address the widespread problem of underassessment and undertreatment of pain."[41] The Joint Commission began incorporating pain management metrics into its accreditation requirements, which again added additional performance incentives surrounding accreditation and quality ratings (more on this below) for providers to approach pain treatment aggressively. Because of these accreditation requirements, some experts believe that the Joint Commission bears a significant share of responsibility for the over-prescribing of opioids.[42]

2.15. *Manufacturer Marketing*. The confluence of increased medical need, heightened emphasis on pain management, and the rise of VBR instruments significantly increased the demand for pain management treatment, including prescription analgesics like

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[39] For example, see generally G. Aston, "Smart pain management makes good business sense," *Hosp Health Netw* 86, no. 6 (2012); A. Gupta et al., "Patient perception of pain care in the United States: a 5-year comparative analysis of hospital consumer assessment of health care providers and systems," *Pain Physician* 17, no. 5 (2014); O. Mazurenko et al., "Predictors of Hospital Patient Satisfaction as Measured by HCAHPS: A Systematic Review," *J Healthc Manag* 62, no. 4 (2017); C. A. Thiels et al., "Achieving a 5-star rating: Analysis of Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) scores among patients undergoing elective colorectal operations," *Surgery* 160, no. 4 (2016).

[40] J. A. Dalton et al., "Clinical economics: calculating the cost of acute postoperative pain medication," *J Pain Symptom Manage* 19, no. 4 (2000). Moreover, the "street value" of opioids was also relatively low compared to other illicit drugs; see generally N. Dasgupta et al., "Crowdsourcing black market prices for prescription opioids," *J Med Internet Res* 15, no. 8 (2013).

[41] D.W. Baker, "The Joint Commission's Pain Standards: Origins and Evolution," (Oakbrook Terrace, IL: The Joint Commission, 2017).

[42] See generally D. W. Baker, "History of The Joint Commission's Pain Standards: Lessons for Today's Prescription Opioid Epidemic," *Jama* 317, no. 11 (2017); "The Joint Commission and the Opioid Epidemic-Reply," *Jama* 318, no. 1 (2017); N. Chhabra and J. B. Leikin, "The Joint Commission and the Opioid Epidemic," ibid.; R. Hirsch, "The Opioid Epidemic: It's Time to Place Blame Where It Belongs," *Mo Med* 114, no. 2 (2017).

opioids.[43] At approximately the same time, there is clear evidence that some manufacturers of opioids began aggressively marketing the products to physicians and promoting them to medical societies.[44] These practices fed into a provider community eager to adopt new means by which to control patient pain, bolstered by CPGs calling for better control of pain and incentive-based payment mechanisms financially rewarding better pain control and higher patient satisfaction. Moreover, there is broad evidence that providers generally respond to such marketing and influence.[45] This type of "supplier induced demand" aligned with the messaging from government agencies, public and private payers, accreditation agencies, and medical societies, all of which progressed unchecked for over a decade. As discussed earlier, the FDA largely failed to act on early indications that such marketing practices were taking place.[46] In addition, large national independent distributors, such as McKesson and Cardinal Health, were aware (via their large national databases) of sharp increases in supply but were focused instead on long-term contracts with manufacturers.

2.16. Manufacturer marketing tactics created a "supply push" that coincided with the "demand pull" fueled by medical need, government advocacy, provider advocacy, and quality ratings. This confluence of these factors further increased overall demand for opioids and to some extent shifted prescribing patterns among physicians from non-opioid to opioid-based treatments.[47] At the same time, manufacturers increased supply and kept prices low to meet the rising demand. In sum, there is little debate as to whether manufacturers employed these tactics to increase opioid sales, and many experts consider the actions of manufacturers as the primary contributing factor in the growth of opioid

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[43] See generally M. Daubresse et al., "Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000-2010," *Med Care* 51, no. 10 (2013); A. Stokes et al., "Trends in Prescription Analgesic Use Among Adults With Musculoskeletal Conditions in the United States, 1999-2016," *JAMA Netw Open* 2, no. 12 (2019).

[44] See generally S. E. Hadland, M. S. Krieger, and B. D. L. Marshall, "Industry Payments to Physicians for Opioid Products, 2013-2015," *Am J Public Health* 107, no. 9 (2017); S. E. Hadland et al., "Association of Pharmaceutical Industry Marketing of Opioid Products With Mortality From Opioid-Related Overdoses," *JAMA Netw Open* 2, no. 1 (2019); A. Alpert et al., "Origins of the Opioid Crisis and its Enduring Impacts," in *NBER Working Paper No. 26500* (National Bureau of Economic Research, 2019); J. H. Marks, "Lessons from Corporate Influence in the Opioid Epidemic: Toward a Norm of Separation," *J Bioeth Inq* 17, no. 2 (2020). Also see S. Spithoff et al., "Drivers of the opioid crisis: An appraisal of financial conflicts of interest in clinical practice guideline panels at the peak of opioid prescribing," *PLoS One* 15, no. 1 (2020). For detailed narrative on this topic, also refer to B. Macy, *Dopesick* (New York, NY: Little, Brown and Company, 2018).

[45] See generally L. Agha and D. Zeltzer, "Drug Diffusion Through Peer Networks: The Influence of Industry Payments," in *NBER Working Paper No. 26338* (National Bureau of Economic Research, 2020); D. Kenkel and A. Mathios, "Promotion to Physicians and Consumers," in *The Economics of the Biopharmaceutical Industry*, ed. P.M. Danzon and S. Nicholson (Oxford, UK: Oxford University Press, 2012).

[46] Kolodny, "How FDA Failures Contributed to the Opioid Crisis."

[47] V. Jairam et al., "Temporal Trends in Opioid Prescribing Patterns Among Oncologists in the Medicare Population," *J Natl Cancer Inst* 113, no. 3 (2021).

prescriptions and sales.[48] Indeed, manufacturers were among the first group of entities to have been found liable and have already paid more than $32 billion in settlements.[49]

2.17. *Macroeconomic Factors*. There is no debate that economic factors in the U.S. played a prominent and unprecedented role in opioid utilization and OUD. As economists Case and Deaton argue in their book *Deaths of Despair and the Future of Capitalism*, "deaths of despair [i.e., those associated with drugs, alcohol, and suicide] are prevalent among those who have been left behind."[50] Throughout the U.S., during the past several decades there have been significant shifts in the structure of the economy, characterized predominantly by a decline in economic activity related to industrial manufacturing, agriculture, energy, and mining,[51] and corresponding rapid growth in high-technology and service industries, such as semi-conductors, telecommunications, information systems, and healthcare. However, overall, net inflation adjusted household incomes rose at the lowest pace in decades, contributing to higher levels of disparities in income and wealth.[52] Moreover, the geographic distribution of these opposing economic trends was largely uneven over this period, as some regions of the U.S. gained (e.g., those with large urban areas and technology corridors with highly trained labor forces) and other regions lost (e.g., those heavily dependent on manufacturing, mining, and agriculture).[53]

2.18. In general, economic hardship has been shown to be a significant driver of mental health, substance abuse, and substance use disorder ("SUD").[54] Indeed, the regions of the U.S. that suffered disproportionately from the economic shift were shown to have increasing rates of depression and substance abuse.[55] Thus, it is not surprising that early indicators of opioid misuse first became apparent in the regions of the country that were least able to adapt their labor forces to growth industries and were, consequently,

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[48] See, for example, R. L. Haffajee and M. M. Mello, "Drug Companies' Liability for the Opioid Epidemic," *N Engl J Med* 377, no. 24 (2017).

[49] See generally O. Dyer, "Drug distributors and Johnson & Johnson will pay $26bn as America's biggest opioid settlement is finalised," *Bmj* 376 (2022); "Opioid lawsuits: Sackler family agree final $6bn civil settlement with US states," *Bmj* 376 (2022).

[50] Case and Deaton, *Deaths of Despair and the Future of Capitalism*. Also see N. Dasgupta, L. Beletsky, and D. Ciccarone, "Opioid Crisis: No Easy Fix to Its Social and Economic Determinants," *Am J Public Health* 108, no. 2 (2018).

[51] These industries are typically thought to have been most impacted (negatively) by "globalization," which is the migration of certain industries and jobs to countries with lower wages and benefits. See generally J. Stiglitz, *Globalization and its Discontents* (New York, NY: W.W. Norton & Co., 2002).

[52] See generally R.J. Gordon, *The Rise and Fall of American Growth: The U.S. Standard of Living Since the Civil War* (Princeton, NJ: Princeton University Press, 2016).

[53] See generally R. Florida, "America's Worsening Geographic Inequality," (Bloomberg News, 2018).

[54] For example, see K. Baptiste-Roberts and M. Hossain, "Socioeconomic Disparities and Self-reported Substance Abuse-related Problems," *Addict Health* 10, no. 2 (2018); P. Pratap et al., "Public Health Impacts of Underemployment and Unemployment in the United States: Exploring Perceptions, Gaps and Opportunities," *Int J Environ Res Public Health* 18, no. 19 (2021). For an in-depth narrative on this topic also see Case and Deaton, *Deaths of Despair and the Future of Capitalism*.

[55] See generally J. Sareen et al., "Relationship Between Household Income and Mental Disorders: Findings From a Population-Based Longitudinal Study," *Archives of General Psychiatry* 68, no. 4 (2011).

experiencing rising rates of depression and substance abuse.[56] Opioid misuse generally followed a pattern of diffusion analogous to other forms of substance abuse, with a timeline and geographic dispersion that aligned with shifts in the economic base.[57] In sum, it is clear that these factors played a very important role, certainly one that exacerbated the impact and actions of other factors.

3. ECONOMICS OF EXTERNALITIES

3.1. In the field of economics, "externalities occur because economic agents have effects on third parties that are not reflected in market transactions."[58] Externalities can exert positive effects (i.e., benefits) or negative effects (i.e., costs) on third parties; positive effects are referred to as "positive externalities" and negative effects are referred to as "negative externalities." The economics sub-fields of environmental economics and public health economics offer commonly cited examples of such externalities. In public health economics, an example of a positive externality is "herd immunity" from vaccinations, where the benefits of vaccines indirectly accrue to the unvaccinated and increase the overall utility of immunization. An example of a negative externality in public health is industrial contamination of shared supplies of potable water. In environmental economics, an example of a positive externality is a farmer who grows apples trees that benefit the pollination needs of bees from a nearby beekeeper. An example of a negative externality is pollution (e.g., soil, water, or air) caused by "factors of production" (e.g., factories, transportation, etc.) that negatively affect "public goods"[59] or otherwise impose some cost on a group of individuals.[60]

3.2. Returning to the case of negative externalities in public health, other examples include alcohol misuse and tobacco use. Alcohol misuse has been shown to result in negative externalities associated with a variety of costs extending beyond those directly consuming it, such as domestic problems, assaults, motor vehicle accidents, financial distress, and

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[56] P. S. Sullivan et al., "The Geography of Opioid Use Disorder: A Data Triangulation Approach," *Infect Dis Clin North Am* 34, no. 3 (2020).

[57] A. Hollingsworth, C. J. Ruhm, and K. Simon, "Macroeconomic conditions and opioid abuse," *J Health Econ* 56 (2017); Compton and Jones, "Epidemiology of the U.S. opioid crisis: the importance of the vector."

[58] W. Nicholson and C. Snyder, *Microeconomic Theory: Basic Principles and Extensions, 12th Edition* (Cengage Learning, 2016).

[59] In economics, the concept of "public goods" refer to goods that were "non-rivalrous" (i.e., consumption by one person does not leave less for another person) and "non-excludable" (i.e., it would be cost-prohibitive to exclude non-paying beneficiaries). Shared environmental resources, such as air, soil, and water, are commonly cited examples of public goods.

[60] In general, a "negative externality" refers to a cost incurred by entities that are not party to the transaction that is contributing to a cost or harm. The most common example is pollution. If the production of a product or service produces pollution, the costs of that pollution is in some cases not incurred solely by the parties to the transaction (e.g., a steel producer selling steel to a construction company), but is instead released into the air or soil, resulting in costs incurred by a larger group. See generally A.A. Papandreou, *Externality and Institutions* (Oxford, UK: Clarendon Press, 1994); R. Cornes and T. Sandler, *The Theory of Externalities, Public Goods, and Club Goods* (Cambridge, UK: Cambridge University Press, 1986); R.H. Coase, "The Problem of Social Cost," *Journal of Law and Economics* 3 (1960).

property damage.[61] Generally, from an economics perspective, OUD can be considered a negative externality associated with the misuse of opioids. More specifically, prescription opioids can be thought of as a factor of production in the "production" of pain management, and OUD can be considered a negative externality attributable in part to the misuse of one of the factors of production. It is also important to note that OUD is also attributable to the use or diverted prescription opioids and illicit opioids, so it is a negative externality resulting from two distinct pathways.

3.3. However, comparisons of OUD with other known public health externalities (like alcohol and tobacco) and environmental externalities (like pollution) should be made with an understanding of two very important caveats. First, whereas OUD is the result of opioid misuse, it is not necessarily the result of *prescription* opioid misuse. This fact limits the classifying of prescription opioids as a source of the externality. Second, unlike alcohol and tobacco, which are minimally regulated, prescription drugs in the U.S. are heavily regulated, including an extensive approval and post-market surveillance process from the FDA and laws governing the legal production of drug prescriptions from licensed healthcare professionals. Third, oversight from the U.S. Drug Enforcement Administration ("DEA"), which is responsible for establishing production quotas for all Schedule I or II controlled substances.[62] Thus, insofar as OUD is a negative public health externality, it is one with multiple and multifactorial sources and one that has been contributed to by the same governmental organizations tasked with regulating prescription drugs externalities.

3.4. Economists have described specific remedies and policy instruments to address negative externalities, including taxes, regulation, bargaining, and courts.[63] Generally, the implementation of such remedies requires four primary sources of information: (1) documentation that a negative externality has resulted in a measurable harm or cost that is "external" to the transaction;[64] (2) the identification of parties responsible for the "production" of the negative externality (e.g., in the case of carbon dioxide, it is not caused by a single factory but multiple factories, and not a single vehicle but multiple vehicles, etc.); (3) a calculation of the costs associated with the abatement of the externality; and

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[61] See generally T. K. Greenfield et al., "Externalities from alcohol consumption in the 2005 US National Alcohol Survey: implications for policy," *Int J Environ Res Public Health* 6, no. 12 (2009).

[62] According to the DEA, Schedule I refers to "drugs with no current medical use with high potential for abuse and/or addiction," and Schedule II refers to "drugs with some medically acceptable uses, but with high potential for abuse and/or addiction." See generally https://www.dea.gov/drug-information/drug-scheduling.

[63] See generally R.D. Cooter and T. Ulen, *Law and Economics (6th Edition)* (Pearson, 2011); Papandreou, *Externality and Institutions*; D.J. Phaneuf and T. Requate, *A Course in Environmental Economics: Theory, Policy, and Practice* (Cambridge, UK: Cambridge University Press, 2017); Cornes and Sandler, *The Theory of Externalities, Public Goods, and Club Goods*.

[64] Again, this follows from the definition of an externality. A harm that is considered "internal" to the transaction is one directly associated with the transaction; for example, if I purchase all the available tickets to a show, others will not be able to attend the show. In contrast, if a factory produces steel that I purchase to build a building, while my transaction with the factory is considered "internal," like the ticket purchases, the factory's emissions of pollution into the air is "external" to the transaction and would thus be considered an externality.

(4) a mechanism by which to allocate liability (and associated abatement costs) among responsible parties.

3.5. The first of these four types of information (i.e., that OUD has resulted in some degree of measurable cost) has been studied extensively. While there is important debate as to the *extent* of opioid-attributable costs, and considerable discussion as to which entities have incurred the such costs, OUD-attributable costs are generally believed to exist.[65] Given that this report is focused on contributing factors, the remainder of the report is concentrated on the identification of responsible parties (item 2 above), and implications to Montgomery County of the liability component of the economics of externalities.

4. RESPONSIBLE PARTIES

4.1. In analyses of negative externalities, economists have described the case of "multi-causality," where more than one entity causes or contributes to the negative externality.[66] One area in which economists have studied multi-causal externalities is soil and air pollution. For example, in the U.S. certain contaminated sites (e.g., "Superfund" sites) in some cases require abatement, and the costs of that abatement are generally allocated among those found responsible for polluting the site.[67] The Comprehensive Environmental Response, Compensation and Liability Act ("CERCLA"), more commonly known as the "Superfund Law," involves the identification of "potentially responsible parties" ("PRPs") associated with contaminated sites, where each PRP is responsible for their share of the estimated attributable cost. In such cases, liability is often assigned retroactively. In addition, in some cases, some identifiable PRPs are insolvent (or otherwise no longer exist) or, in the case of responsible government agencies, protected by immunity. In such cases, "absent" PRPs can still be allocated some portion of responsibility, typically referred to as "orphan shares."[68]

4.2. Regardless of the approach to liability allocation, the idea that liability should to some extent be allocated to both present and absent defendants is well established. This is an important consideration when discussing the primary causative factors of opioid utilization, as many of these factors could be thought of as bearing "orphan shares" of responsibility, not necessarily due to insolvency or non-existence, as in the typical

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[65] See, for example, S. Davenport, A. Weaver, and M. Caverly, "Economic Impact of Non-Medical Opioid Use in the United States: Annual Estimates and Projections for 2015 through 2019," (Schaumburg, IL: Society of Actuaries, 2019); C. Florence, F. Luo, and K. Rice, "The economic burden of opioid use disorder and fatal opioid overdose in the United States, 2017," *Drug Alcohol Depend* 218 (2021).

[66] See, for example, section 10.6 ("Multi-Causality"; p.257-258) of Phaneuf and Requate, *A Course in Environmental Economics: Theory, Policy, and Practice*.

[67] See generally L. Priya, G. K. Varghese, and I. K. Shah, "Liability allocation in pollution involving multiple responsible parties," *Environ Sci Pollut Res Int* 27, no. 36 (2020). Also see section 10.7 ("Examples of Environmental Liability Laws" p. 258-261) of Phaneuf and Requate, *A Course in Environmental Economics: Theory, Policy, and Practice*.

[68] See generally K. K. Kilbert, "Neither Joint Nor Several: Orphan Shares in Private CERCLA Actions," *Environmental Law* 41, no. 4 (2011).

CERCLA application, but instead due to "atomistic" distribution (e.g., hundreds of thousands of physicians or patients), "diffuse" nature (e.g., organizations excessively promoting pain management), or "sovereign immunity" (e.g., government and regulatory agencies). Hall et al. describe the problem this way: "The problem [of allocation] is aggravated by the presence of 'orphan' shares, which are the shares left by absent or insolvent PRPs that must be allocated among the rest of the group. Often these 'orphan' shares are substantial, including former owners and operators who had a major role in the mismanagement of the hazardous waste giving rise to the problem, but who are not available to pay for the cleanup."[69]

4.3. PRPs are to be distinguished from "contributing factors." The contributing factors described above in Section 2 are *factors* which, according to the large literature on opioid supply, enabled, caused, or directly contributed to the supply of prescription opioids. In the case of PRPs, we are interested in the identifiable *entities* that enabled, caused, or directly contributed to the supply of prescription opioids. That said, in many cases, discussion of contributing factors directly or indirectly implies specific PRPs. For example, "macroeconomic" factors-- while undeniably important drivers of SUD, opioid utilization, and opioid misuse-- do not directly constitute an identifiable PRP. However, macroeconomic factors exacerbated drug seeking behavior by individuals, which in turn magnified the contributing role of physicians and drug traffickers. In addition, the impact of macroeconomic factors, which was generally well known by economists and policy experts, could have been more effectively mitigated by federal and state governmental agencies.

4.4. Applying this logic to each of the contributing factors, the alignment of PRPs and contributing factors is shown in Figure 4-1. Again, because the plaintiffs have based their arguments on an alleged causative linkage between opioid supply and opioid costs, the figure maps the contributing factors into PRPs, and then maps the PRPs into two categories of opioid supply: supply of prescription opioids and supply of non-prescription opioids. Together, these two categories constitute the total supply of opioids in the U.S.

4.5. As shown in Figure 4-1, the previously discussed contributing factors to opioid supply map to the following PRPs: (1) FDA; (2) DEA; (3) CDC; (4) Physicians;[70] (5) Health Systems; (6) Patients; (7) Federal government; (8) State government; (9) Accreditation agencies; (10) Payers; (11) Manufacturers; (12) Distributors; and (13) Drug traffickers. Note that drug traffickers are added here because the goal in the context of the economics of externalities is to identify entities that have contributed or caused opioid supply. Drug traffickers are entities causing supply of non-prescription opioids; hence, I make that distinction in Figure 4-1.

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[69] R.M. Hall, R.H. Harris, and J.A. Reinsdorf, "Superfund Response Cost Allocations: The Law, The Science and The Practice," *The Business Lawyer (American Bar Association)* 49, no. 4 (1994).

[70] In Figure 4-1, the term "Providers" collectively refers to all licensed prescribers (i.e., clinicians, mainly physicians and physician extenders such as physician assistants and nurse practitioners) and health systems (i.e., hospitals, emergency departments, outpatient clinics), which often advise and guide clinicians on preferred practices via clinical pathways and clinical practice guidelines.

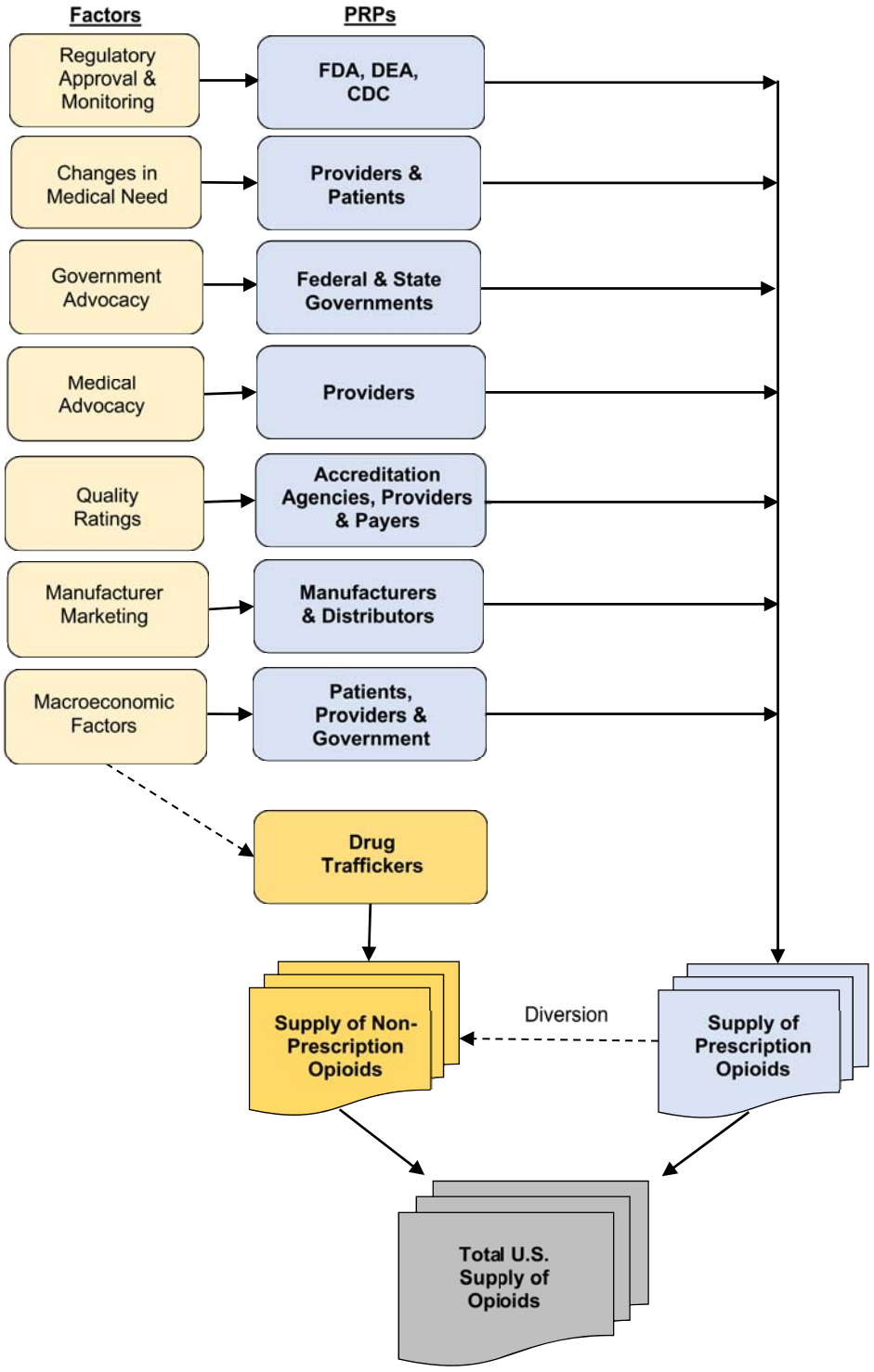

Figure 4-1. Contributing Factors and Potentially Responsible Parties Associated with Prescription Opioid Supply and Non-Prescription Opioid Supply. *Notes*: PRP = Potentially Responsible Party; FDA= U.S. Food & Drug Administration; DEA = U.S. Drug Enforcement Administration; CDC = Centers for Disease Control & Prevention; "Providers" refers to physicians and health systems

4.6. *FDA*. As discussed in Section 2, the FDA is a PRP for two reasons: (1) initial approval of long-acting opioids, which was viewed by manufacturers, physicians, and patients as a "stamp of approval;" and (2) subsequent failure to perform sufficient post-market surveillance and monitoring. While the FDA is a regulatory agency within the federal government (which is also identified as a PRP), I identify it as a separate PRP due to its direct remit to regulate prescription drugs.

4.7. *DEA*. The DEA is a PRP for two reasons: (1) failure to use prescription drug production quotas[71] and other monitoring functions to detect, manage, or mitigate opioid supply concerns; and (2) failure to effectively control or mitigate the influx of illicit opioids. A report by the U.S. Office of the Inspector General ("OIG") published in 2019 was very critical of the DEA's actions regarding opioids, concluding that "…DEA was slow to respond to the significant increase in the use and diversion of opioids since 2000" and "did not use its available resources, including its data systems and strongest administrative enforcement tools, to detect and regulate diversion effectively."[72] The OIG report also found that "DEA policies and regulations did not adequately hold registrants accountable or prevent the diversion of pharmaceutical opioids." Like the FDA, the DEA failed in its role as regulator and monitor of prescription opioid diversion and illicit opioid intrusion. Again, while the DEA is a regulatory agency within the federal government (which is also identified as a PRP), I identify it as a separate PRP due to its direct remit to regulate prescription and non-prescription drugs.

4.8. *CDC*. Whereas it is the FDA's remit to approve prescription drugs, it is the CDC's mission to prevent, control, and manage outbreaks, epidemics, and pandemics, describing their mission as: "…to protect America from health, safety, and security threats […] CDC fights disease and supports communities and citizens to do the same."[73] Some observers view opioid use and misuse as an "epidemic,"[74] the origins of which began in the late 1990s following the approval and diffusion of long-acting opioids. It has been and continues to

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[71] The U.S. DEA Administrator is "required to set individual quotas for each registered manufacturer seeking to produce such substances and to limit or reduce individual quotas as necessary to prevent oversupply." See CRS, "The Controlled Substances Act (CSA): A Legal Overview for the 117th Congress," (Washington, D.C.: United States Congressional Research Service, 2021). (p.15); also see generally DEA, "DEA reduces amount of opioid controlled substances to be manufactured in 2017," (United States Drug Enforcement Administration, 2016). The GAO found the DEA deficient in effectively carrying out its role in monitoring prescription drugs generally and opioids specifically; see generally GAO, "Drug Shortages: Better Management of the Quota Process for Controlled Substances Needed; Coordination between DEA and FDA Should Be Improved," in *GAO-15-202* (Washington, D.C.: U.S. Government Accountability Office 2015).

[72] OIG, "Review of the Drug Enforcement Administration's Regulatory and Enforcement Efforts to Control the Diversion of Opioids," in *Evaluation and Inspections Division 19-05* (Washington, D.C.: United States Department of Justice; Office of the Inspector General 2019).

[73] Refer to https://www.cdc.gov/about/organization/mission.htm.

[74] I am not offering an opinion as to whether opioid misuse constitutes an "epidemic." However, plaintiffs in opioid matters typically refer to opioid misuse as an epidemic.

be the remit of the CDC to monitor any developing public health problem, especially one that some observers have termed an epidemic. However, it was not until 2016 that the CDC issued guidelines on opioid prescribing, four years *after* the precipitous decline in opioid prescriptions had already begun.[75] That delay has resulted in some experts and observers faulting the CDC for their delayed response.[76] The CDC was similarly faulted for their slow and poorly coordinated response to the Covid-19 pandemic, prompting its director to declare that "…in our big moment, our performance did not reliably meet expectations."[77] Hence, the CDC is a PRP for two reasons: (1) regarding opioids, generally failing in its role in identifying, tracking, and mitigating "epidemics" in the U.S.; and (2) generally failing to provide an effective, timely mitigation solution (e.g., prescribing guidelines were released in 2016, 20 years after OxyContin was approved by the FDA).

4.9. *Physicians*. As a condition of licensure, practicing physicians are professionally and legally responsible for the safety and quality of care provided to their patients. For example, in the American Medical Association's ("AMA") "Declaration of Professional Responsibility" the first obligation is to "treat the sick and injured with competence and compassion and without prejudice," and to "apply our knowledge and skills when needed, though doing so may put us at risk."[78] As shown in Figure 4-2, the medical literature indexing database "PubMed" identifies about 400 articles published per year with keywords "opioid abuse" from 1973 to 2000, with the number increasing sharply thereafter. Thus, during this time it would be reasonable to assume that the medical community, including provider groups and specialty societies, were aware of the risks and tradeoffs associated with opioid use and misuse yet continued to prescribe opioids.[79] Indeed, presumed medical knowledge on the part of opioid prescribing physicians contributed to several criminal cases filed against "high volume" prescribers.[80] Physicians

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[75] See generally D. Dowell, T. M. Haegerich, and R. Chou, "CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016," *Jama* 315, no. 15 (2016); Goldstick et al., "Changes in Initial Opioid Prescribing Practices After the 2016 Release of the CDC Guideline for Prescribing Opioids for Chronic Pain."; Gumidyala et al., "Effect of CDC Opioid-Prescribing Guidelines in a Community Hospital Emergency Department."; J. V. Pergolizzi, Jr., M. Rosenblatt, and J. A. LeQuang, "Three Years Down the Road: The Aftermath of the CDC Guideline for Prescribing Opioids for Chronic Pain," *Adv Ther* 36, no. 6 (2019).

[76] M. Szalavitz, "We're Overlooking a Major Culprit in the Opioid Crisis: Pharmaceutical Companies and Drug Dealers Have Been Part of the Problem—But So Have Policy Makers," *Scientific American* May 28 (2021).

[77] K. Mahr, "CDC director orders agency overhaul, admitting flawed Covid-19 response," *Politico* August 17 (2022).

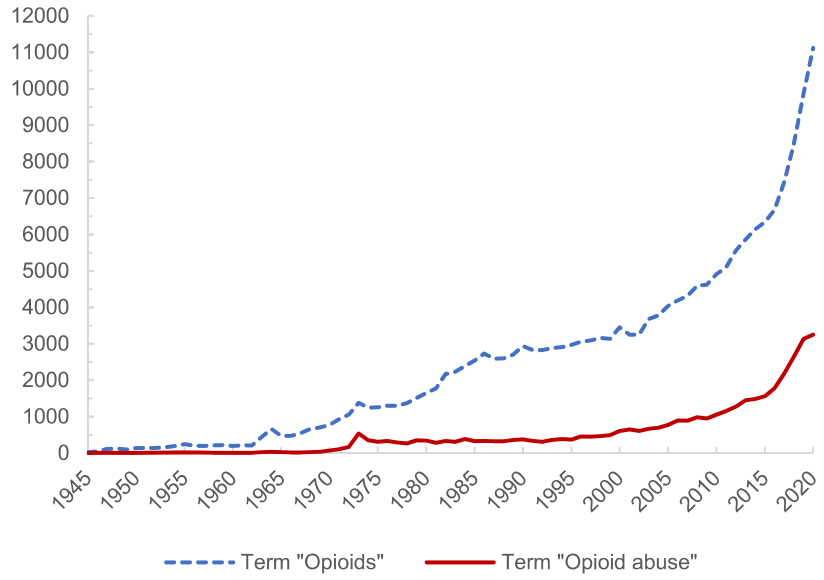
[78] https://www.ama-assn.org/delivering-care/public-health/ama-declaration-professional-responsibility

[79] See generally J. M. DuBois et al., "A Mixed-Method Analysis of Reports on 100 Cases of Improper Prescribing of Controlled Substances," *J Drug Issues* 46, no. 4 (2016); W. G. LeBrett et al., "High Opioid Prescribing Profiles Among Gastroenterologists: A Nationwide Analysis," *Clin Gastroenterol Hepatol* (2021); A. N. Romman et al., "Opioid Prescribing to Medicare Part D Enrollees, 2013-2017: Shifting Responsibility to Pain Management Providers," *Pain Med* 21, no. 7 (2020); B.M. Gray et al., "Clinical Knowledge and Trends in Physicians' Prescribing of Opioids for New Onset Back Pain, 2009-2017," *JAMA Network Open* 4, no. 7 (2021).

[80] See generally J. B. Berman and G. Li, "Characteristics of criminal cases against physicians charged with opioid-related offenses reported in the US news media, 1995-2019," *Inj Epidemiol* 7, no. 1 (2020); C. S.

themselves have admitted fault in over-prescribing opioids.[81] Moreover, providing additional evidence of the influence of published literature and CPGs, prescribing patterns later moved away from opioids when CPGs began incorporating language cautioning providers on potential for misuse.[82] It is also important to note that physician prescribing of opioids, when combined with the incentives associated with quality ratings employed by accreditation agencies and payers, resulted in physician *organizations*, such as medical groups, hospitals and health systems, directly encouraging the use of opioids in pain management.[83]

Figure 4-2. Number of Publications Indexed on PubMed Related to Opioids and Opioid Abuse, 1945-2020



4.10. Physicians are PRPs for four reasons: (1) initiating *all* appropriate and inappropriate opioid prescriptions, some proportion of which was in response to greater medical need, greater perceived medical need, and patient drug-seeking behavior; (2) allowing clinical judgement to be influenced or altered due to manufacturer marketing; (3) allowing clinical judgement to be influenced or altered by state medical boards and provider advocacy groups emphasizing importance of pain management; and (4) allowing clinical judgement

Davis and D. H. Carr, "Self-regulating profession? Administrative discipline of "pill mill" physicians in Florida," *Subst Abus* 38, no. 3 (2017).

[81] See generally S. Chouinard, A. Prasad, and R. Brown, "Survey Assessing Medical Student and Physician Knowledge and Attitudes Regarding the Opioid Crisis," *Wmj* 117, no. 1 (2018); K. Theisen et al., "The United States opioid epidemic: a review of the surgeon's contribution to it and health policy initiatives," *BJU Int* 122, no. 5 (2018).

[82] See generally Gray et al., "Clinical Knowledge and Trends in Physicians' Prescribing of Opioids for New Onset Back Pain, 2009-2017."; Goldstick et al., "Changes in Initial Opioid Prescribing Practices After the 2016 Release of the CDC Guideline for Prescribing Opioids for Chronic Pain."

[83] See, for example, O. Mazurenko et al., "Clinical perspectives on hospitals' role in the opioid epidemic," *BMC Health Serv Res* 20, no. 1 (2020).

to be influenced or altered by accreditation agencies, health systems and payers prioritizing pain management in quality ratings and performance assessment.

4.11. *Health Systems*. The group identified as "health systems" includes providers with some degree of vertical integration (i.e., the combing of "upstream" and "downstream" inputs and services). These can be community hospitals with affiliated outpatient feeders, larger health systems with multiple hospitals and outpatient feeders, and integrated delivery networks ("IDNs") which provide the full continuum of services and are able to underwrite some degree of financial risk (which may also include Accountable Care Organizations, or "ACOs"). Examples of large IDNs in the U.S. include HCA Healthcare, Ascension Health, and Intermountain Health. Health systems are primary PRPs for four reasons: (1) failure to monitor and control prescribing patterns of member physicians; (2) allowing incentive payments from opioid manufacturers to influence protocols and prescribing patterns of member physicians;[84] (3) allowing clinical judgement of physician members to be influenced or altered by state medical boards and provider advocacy groups emphasizing prioritization of pain management;[85] and (4) allowing clinical judgement of physician members to be influenced or altered by accreditation agencies and payers prioritizing pain management in quality ratings, performance assessment, and value-based reimbursement.

4.12. *Patients*. I use the term "patients" to refer generally to individuals who have been prescribed opioids, given that the focus of this report is the role of prescription opioids. However, my use of the term also includes individuals who unlawfully obtain prescription opioids from the patients to whom the drugs were prescribed or from drug traffickers, as these individuals (and their associates) then *de facto* become opioid misusers. Patients who knowingly misuse opioids or facilitate misuse among others violate laws regarding use of prescription medications and the implicit contract[86] regarding responsible and proper use of prescription drugs. Patients are more likely to be materially involved in opioid diversion compared to other types of drug diversion, including intentionally seeking prescriptions from doctors and hospital emergency departments for non-medical use or improperly obtaining opioids from family and friends, including theft. For example, one comprehensive study found that 94% of opioids intentionally sought for non-medical use were obtained from either family and friends, a single doctor, drug dealers, or strangers.[87] Although it is often broadly argued that patients are less able to make informed

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[84] See generally T. S. Anderson et al., "Financial Payments to Teaching Hospitals by Companies Marketing Opioids," *J Gen Intern Med* 35, no. 10 (2020).

[85] See generally Mazurenko et al., "Clinical perspectives on hospitals' role in the opioid epidemic."

[86] In studies of medication adherence and proper use (and misuse) patient responsibility is often identified as a critical element. This can be seen in the literature on "opioid contracts." See generally J. Hariharan, G. C. Lamb, and J. M. Neuner, "Long-term opioid contract use for chronic pain management in primary care practice. A five year experience," *J Gen Intern Med* 22, no. 4 (2007); J. V. Pergolizzi et al., "A multicentre evaluation of an opioid patient-provider agreement," *Postgrad Med J* 93, no. 1104 (2017); L. Svirsky, "Opioid Treatment Agreements and Patient Accountability," *Hastings Cent Rep* 51, no. 4 (2021).

[87] J. A. Inciardi et al., "The "black box" of prescription drug diversion," *J Addict Dis* 28, no. 4 (2009).

medical care decisions,[88] the same broad argument cannot be used to argue that patients do not bear any responsibility in preventing or deterring opioid misuse. Indeed, diversion laws and opioid contracts clearly imply that patients bear some of the responsibility for proper use of opioids and are responsible for some degree of self-regulation. Thus, patients are considered PRPs for two reasons: (1) when they knowingly engage in opioid diversion or opioid-seeking behavior; and (2) when they engage in opioid misuse or unsecure storage (which in turn may increase the probability of unintentional diversion).

4.13. *Federal Government*. Apart from the specific agency roles of the FDA, DEA, and CDC, the federal government is a primary PRP for five reasons: (1) in its role engaging in direct advocacy of aggressive pain management; (2) promotion of quality ratings and performance-based incentives in the health insurance plans it directly administers [e.g., Medicare; Veterans Health Administration ("VHA")];[89] (3) failing to utilize its own insurance data to monitor opioid usage or control access among its enrollees; and (4) insufficiently monitoring and mitigating the health impact of macroeconomic changes.[90]

4.14. *State Government*. State governments are primary PRPs for reasons similar to those associated with the federal government, including: (1) direct advocacy of aggressive pain management by state medical boards;[91] (2) promotion of quality ratings and performance-based incentives in state health insurance plans (e.g., Medicaid, especially Medicaid Managed Care);[92] (3) failing to utilize its own insurance data to monitor opioid usage or control access among its enrollees; and (d) insufficiently monitoring and mitigating the health impact of macroeconomic changes.

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[88] For a general discission of this refer to A. Coulter, "Partnerships with patients: the pros and cons of shared clinical decision-making," *J Health Serv Res Policy* 2, no. 2 (1997); A. Robinson and R. Thomson, "Variability in patient preferences for participating in medical decision making: implication for the use of decision support tools," *Qual Health Care* 10 Suppl 1, no. Suppl 1 (2001).

[89] Discussed in Section 3.

[90] A 2017 study published in the Harvard Business Review describes the role of government in addressing economic downturn (due to globalization) as follows: "We need to reinvest in dislocated communities, lower the costs and barriers to trade, match smaller firms with foreign markets, match communities with foreign investors, ensure unfettered access to cross-border digital platforms, provide greater safety net measures, update our system of unemployment insurance, provide relocation assistance, encourage portable health insurance, [and] retrain our workers for the new opportunities…" G. Pinkus, J. Manyika, and S. Ramaswamy, "We Can't Undo Globalization, but We Can Improve It," *Harvard Business Review* (2017).As discussed in Section 3, in many areas affected by globalization, most of these policies were not sufficiently implemented, or not implemented at all. See generally Case and Deaton, *Deaths of Despair and the Future of Capitalism*; Gordon, *The Rise and Fall of American Growth: The U.S. Standard of Living Since the Civil War*; Y. Ding et al., "How Does Government Efficiency Affect Health Outcomes? The Empirical Evidence from 156 Countries," *Int J Environ Res Public Health* 19, no. 15 (2022).

[91] See generally A. M. Gilson, D. E. Joranson, and M. A. Maurer, "Improving state pain policies: recent progress and continuing opportunities," *CA Cancer J Clin* 57, no. 6 (2007); A. M. Gilson, M. A. Maurer, and D. E. Joranson, "State policy affecting pain management: recent improvements and the positive impact of regulatory health policies," *Health Policy* 74, no. 2 (2005).

[92] See generally P. Rowan et al., "Quality Rating Systems in Medicaid Managed Care," (Washington, DC: Mathematica, 2021).

4.15. *Accreditation Agencies*. As discussed in Section 2, accreditation agencies such as the Joint Commission are primary PRPs for two reasons: (1) requiring, as a condition of accreditation, that providers adopt and maintain aggressive pain management programs; and (2) requiring, as a condition of accreditation, the inclusion of pain control as a separate component of patient satisfaction in quality ratings.

4.16. *Payers*. Above I identified the role of public payers like Medicare and Medicaid in the identification of state and federal governments as PRPs. The same rationale can be applied to private payers, including commercial insurance plans, managed care organizations, and workers compensation payers, all of which were positioned to leverage their own administrative data and claims data to help identify patterns in opioid utilization and misuse. Administrative and claims data form the backbone of payer operations. Such data track most or all interactions an enrollee has with the health system, mainly for the purposes of claims processing and payment. Claims data typically include patient characteristics, primary and secondary diagnosis codes, physician visits, prescription drug orders [including National Drug Code ("NDC"),[93] prescriber, and pharmacy], emergency department visits, and hospitalizations. These data are often used to identify a variety of utilization patterns and adverse events, due mainly to their detail and their ability to link together services provided by multiple providers in multiple settings.[94] Thus, it seems plausible that administrative data could have been used more effectively to identify patients engaging in behavior consistent with misuse and cost-incurring OUD.[95] Additional evidence of this is in the effectiveness of payer-based opioid control initiatives following implementation.[96] Whereas public payers were factors contributing to the role of federal and state governments as PRPs, private payers are PRPs for similar reasons; specifically: (1) supporting direct advocacy of aggressive pain management; (2) promoting the use of quality ratings and performance incentives that financially rewarded network providers for higher patient satisfaction (which is correlated with more aggressive

[93] NDCs are the industry standard means of identifying prescription drugs and consist of a unique 10-digit or 11-digit code with 3 segments: the labeler, the product, and the commercial package size.

[94] See, for example, R. Baron, G. Mick, and M. Serpell, "The relevance of real-world data for the evaluation of neuropathic pain treatments," *Pain Manag* 12, no. 7 (2022); S. S. Dhruva et al., "Attribution of Adverse Events Following Coronary Stent Placement Identified Using Administrative Claims Data," *J Am Heart Assoc* 9, no. 4 (2020); Y. L. Huang, J. Moon, and J. B. Segal, "A comparison of active adverse event surveillance systems worldwide," *Drug Saf* 37, no. 8 (2014); M. Kalinich et al., "Prediction of severe immune-related adverse events requiring hospital admission in patients on immune checkpoint inhibitors: study of a population level insurance claims database from the USA," *J Immunother Cancer* 9, no. 3 (2021).

[95] For example, see S. E. Heins et al., "Claims-based measures of prescription opioid utilization: A practical guide for researchers," *Drug Alcohol Depend* 228 (2021). Indeed, in recent years there have been specific algorithms developed for this purpose. For example, see K. Rough et al., "Using prescription claims to detect aberrant behaviors with opioids: comparison and validation of 5 algorithms," *Pharmacoepidemiol Drug Saf* 28, no. 1 (2019); J. W. Sun et al., "Predicting overdose among individuals prescribed opioids using routinely collected healthcare utilization data," *PLoS One* 15, no. 10 (2020).

[96] For example, see M. C. García et al., "Declines in Opioid Prescribing After a Private Insurer Policy Change - Massachusetts, 2011-2015," *MMWR Morb Mortal Wkly Rep* 65, no. 41 (2016); T. Molfenter et al., "The payer's role in addressing the opioid epidemic: It's more than money," *J Subst Abuse Treat* 101 (2019); S. Shen et al., "The implementation of opioid prescribing report cards in Medicaid managed care: a community quality collaborative," *Am J Manag Care* 27, no. 12 (2021).

pain management); and (3) failing to utilize administrative and claims data to monitor opioid usage or control access.

4.17. *Manufacturers*. As discussed in Section 2, manufacturers are primary PRPs for two reasons: (1) aggressive opioid marketing tactics aimed at medical societies, physicians, and health systems; and (2) failure to fully disclose evidence regarding the risks or opioid misuse (i.e., OUD; addiction). Manufacturers have already been found liable in some jurisdictions.

4.18. *Distributors*. Three large national, independent wholesale distributors of healthcare products control more than 85% of the drug distribution market: Cardinal Health, McKesson, and AmerisourceBergen.[97] Large independent wholesale distributors are primary PRPs for two reasons: (1) deferring to manufacturers, with whom a small number of large wholesale distributors maintain long-term contracts; and (2) "failing to diligently respond to suspicious orders."[98]

4.19. *Drug Traffickers*. Drug trafficking is defined broadly as "…the illegal transporting of or transacting in controlled substances."[99] Under federal law, Title 21 (§ 841) makes it unlawful for any person to knowingly or intentionally "manufacture, distribute, or dispense, or possess with intent to manufacture, distribute, or dispense, a controlled substance." Thus, the group "drug traffickers" includes not only criminals involved in the "business" of illicit drug manufacturing and distributing, but also individuals and patients who knowingly divert controlled substances for non-medical use. There is evidence that illegally trafficked illicit opioids (heroin and fentanyl) have contributed disproportionately to OUD and opioid overdoses.[100] In recent years there has been a substantial increase in the supply of illicit trafficked and smuggled opioids, sourced mainly from Mexico and Canada (via border crossing) and China (via either direct mail or via Canada or Mexico borders).[101] The DEA estimated that Mexico's heroin production grew from 42 metric tons in 2014 to 106 metric tons in 2018, an increase of 152%.[102] Between 2013 and 2017, the

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[97] KFF, "Follow The Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain," (Menlo Park, CA: Kaiser Family Foundation, 2005).

[98] See generally Haffajee and Mello, "Drug Companies' Liability for the Opioid Epidemic."

[99] Legal Information Institute, "Drug Trafficking," (Ithaca, NY: Cornell Law School, 2021).

[100] See generally V. Felbab-Brown, "Fending off fentanyl and hunting down heroin: Controlling opioid supply from Mexico," in *The Opioid Crisis in America: Domestic and International Dimensions* (Washington, D.C.: Brookings Institution, 2020); C. Fleiz et al., "Fentanyl is used in Mexico's northern border: current challenges for drug health policies," *Addiction* 115, no. 4 (2020); N. G. Shah et al., "The influence of living along the U.S.-Mexico border on unintentional drug overdose death, New Mexico (USA), 2005-2009," *Drug Alcohol Depend* 125, no. 1-2 (2012); USDOJ, "New Mexico High Intensity Drug Trafficking Area," in *Drug Market Analysis 2011* (U.S. Department of Justice, National Drug Intelligence Center, 2011); L. C. Dismukes, "How Did We Get Here? Heroin and Fentanyl Trafficking Trends: A Law Enforcement Perspective," *N C Med J* 79, no. 3 (2018).

[101] GAO, "Illicit Opioids: While Greater Attention Given to Combating Synthetic Opioids, Agencies Need to Better Assess their Efforts," in *Report to Congressional Requesters* (Washington, D.C.: U.S. Government Accountability Office, 2018).

[102] USDOJ, "2019 National Drug Threat Assessment (NDTA)," (U.S. Department of Justice, Drug Enforcement Administration, 2019).

volume of opioids seized each year increased 96%, from 579 pounds to 1,135 pounds.[103] Some states have been disproportionately affected by illicit opioids. For example, in the Ohio High Intensity Drug Trafficking Areas ("HIDTAs"),[104] the U.S. Department of Justice ("DOJ") reports that "Heroin availability has increased in the Ohio HIDTA region because of an increased supply of Mexican heroin. Increased heroin trafficking has resulted in a rise in heroin abuse and heroin-related crime, leading law enforcement agencies to identify heroin as the greatest drug threat in the region."[105]

4.20. Like the delayed response to rising rates of opioid misuse on the part of the FDA and CDC, the DEA and other law enforcement agencies were slow to react to the increase in trafficking of illicit opioids.[106] For example, delays in testing for illicit fentanyl masked the increasing role of illicit opioids in OUD cases and attributable deaths and led observers to assume (incorrectly) that most of those cases were due to prescription opioids.[107] A study conducted in Massachusetts, for example, found that "of 2,916 decedents with complete toxicology reports, 1,789 (61.4%) had heroin and 1,322 (45.3%) had fentanyl detected in postmortem toxicology reports. Of the 491 (16.8%) decedents with ≥ 1 opioid prescription active on the date of death, prescribed opioids were commonly not detected in toxicology reports."[108] There is little debate that as prescription opioid volume declined precipitously in the past decade (along with rates of misuse attributable to prescription opioids). However, a contemporaneous rise in the role of illicit opioids continued to cause

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[103] HSGAC, "Combating the Opioid Epidemic: The Interception of Illicit Opioids by the Border Patrol," (Washington, D.C.: United States Senate: Committee on Homeland Security & Governmental Affairs, 2018).

[104] According to the DEA, "High Intensity Drug Trafficking Areas (HIDTA) program, created by Congress with the Anti-Drug Abuse Act of 1988, provides assistance to Federal, state, local, and tribal law enforcement agencies operating in areas determined to be critical drug-trafficking regions of the United States. This grant program is administered by the Office of National Drug Control Policy (ONDCP). There are currently 33 HIDTAs." To qualify as an HIDTA, a county must meet the following criteria: (1) The area is a significant center of illegal drug production, manufacturing, importation, or distribution; (2) State, local, and tribal law enforcement agencies have committed resources to respond to the drug trafficking problem in the area, thereby indicating a determination to respond aggressively to the problem; (3) Drug-related activities in the area are having a significant harmful impact in the area and in other areas of the country; and (4) A significant increase in allocation of Federal resources is necessary to respond adequately to drug related activities in the area. See https://www.dea.gov/operations/hidta. Note that Montgomery County, OH, is classified as a HIDTA.

[105] USDOJ, "Ohio High Intensity Drug Trafficking Area," in *Drug Market Analysis 2011* (Washington, D.C.: U.S. Department of Justice, National Drug Intelligence Center, 2011).

[106] See generally GAO, "Illicit Opioids: While Greater Attention Given to Combating Synthetic Opioids, Agencies Need to Better Assess their Efforts." Also see OIG, "Review of the Drug Enforcement Administration's Regulatory and Enforcement Efforts to Control the Diversion of Opioids."

[107] See generally J. O'Donnell et al., "Using death scene and toxicology evidence to define involvement of heroin, pharmaceutical morphine, illicitly manufactured fentanyl and pharmaceutical fentanyl in opioid overdose deaths, 38 states and the District of Columbia, January 2018-December 2019," *Addiction* 117, no. 5 (2022).

[108] A. Y. Walley et al., "The Contribution of Prescribed and Illicit Opioids to Fatal Overdoses in Massachusetts, 2013-2015," *Public Health Rep* 134, no. 6 (2019).

OUD-attributable deaths due to the increased influx and lethality of illicit opioids.[109] Hence, drug traffickers are PRPs for three reasons: (1) increasing overall supply of opioids via unlawful importation, transportation, and distribution; (2) contributing directly to misuse of opioids by directly supplying individuals with SUD, who are more likely to seek illicit drugs;[110] and (3) in the case of patients, knowingly engaging in drug-seeking and diversion behavior.

5. OUD-ATTRIBUTABLE COSTS

5.1. Having identified PRPs associates with the total supply of opioids in the U.S. (i.e., as depicted in Figure 4-1), I now return to the discussion of the economics of externalities to describe the relationship between total opioid supply and the negative externality potentially associated with some proportion of total opioid supply, in the form of rates of OUD. Although the negative externality is OUD, in economics we typically express the negatively externality as a cost. I begin by discussing the pathway between total opioid supply and OUD, as shown in Figure 5-1.

[109] Another way to approach these contemporaneous (and potentially offsetting) effects is via data modelling; for an example of such, see T. Y. Lim et al., "Modeling the evolution of the US opioid crisis for national policy development," *Proc Natl Acad Sci U S A* 119, no. 23 (2022).

[110] See generally A. Gili et al., "Patterns of Prescription Medicine, Illicit Drugs, and Alcohol Misuse among High-Risk Population: A Factor Analysis to Delineate Profiles of Polydrug Users," *Healthcare (Basel)* 10, no. 4 (2022); D. Lewer et al., "Frequency of health-care utilization by adults who use illicit drugs: a systematic review and meta-analysis," *Addiction* 115, no. 6 (2020).

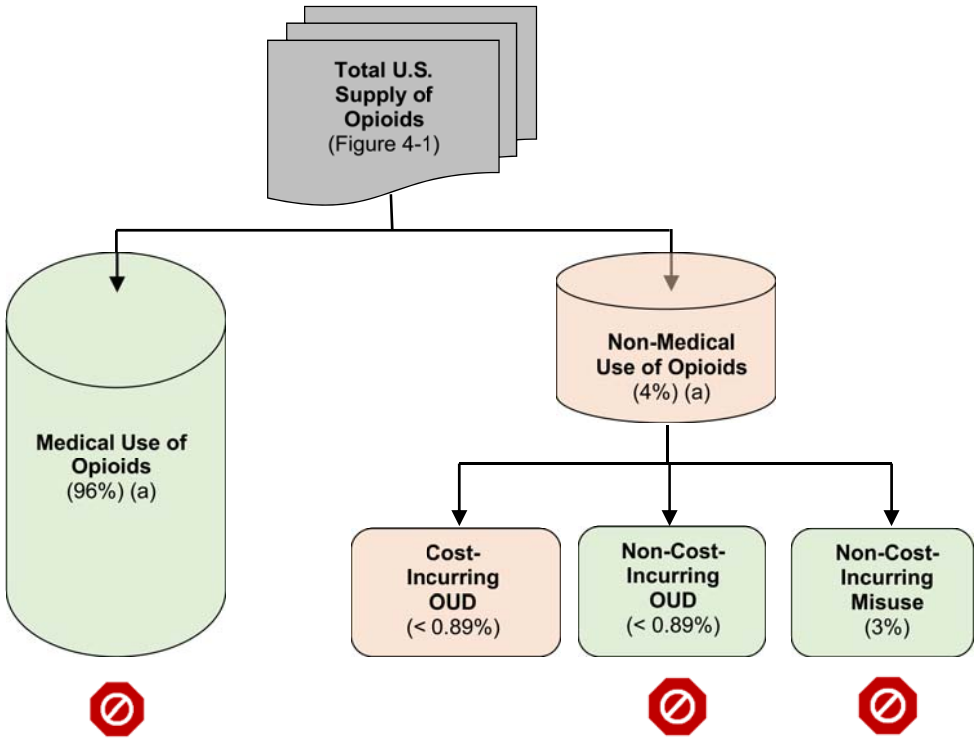

Figure 5-1. Association of Opioid Supply with OUD
Notes: OUD = opioid use disorder (see text for definition)
(a) percentage based on prescription opioids

5.2. Overall, the most important implication of this figure is that, unlike other negative externalities, the "production" of the supply of opioids is *not* the cause of the negative externality. For example, in contrast, it may be the case that the more steel a factory produces, the more pollution is emitted into the air. This is not the case with opioid supply, as the production of supply is not *de facto* contributing to the attributable costs of the externality. As the figure depicts, there are two additional pathways between production and potential attributable costs.

5.3. The first branch of Figure 5-1 distinguishes between opioid supply that is used "as directed" in response to some type of medical need versus non-medical use of opioids. The reason for this distinction is because for the purposes of this matter and others like it, there is no reason to assume that proper medical use of opioids results in any costs. It is important to note that "medical use" does not necessarily require, in the case of prescription opioids, that prescriptions were "medically necessary" (i.e., based on objective measures of medical need). According to the NSDUH data, which is based on a sample of the U.S. population ages 18 and older, the current prevalence of "prescription pain reliever misuse in the past year" is 3.59%.[111] This is broadly consistent with studies

[111] The NSDUH defines "misuse" as "use in any way not directed by a doctor, including use without a prescription of one's own; use in greater amounts, more often, or longer than told; or use in any other way not directed by a doctor." Refer to "2018-2019 NSDUH State Estimates of Substance Use and Mental Disorders," U.S. Substance Abuse and Mental Health Services Administration (SAMHSA).

that use other sources of data. For example, Saha et al. reported a rate of 4.1% based on data from the 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions-III ("NESARC-III").[112] Thus, approximately 96% of prescription opioids are used as directed, and roughly 4% are misused.

5.4. It is also important to note that the misuse branch of the figure is likely to be disproportionately driven by illicit opioids. For example, recall that Walley et al. found that, in a study of about 3,000 OUD decedents with complete toxicology reports, 61.4% had heroin and 45.3% had fentanyl detected in postmortem toxicology reports, and among the 16.8% decedents with one or more active opioid prescriptions on the date of death, prescribed opioids were rarely detected in toxicology reports.[113]

5.5. Also note that the 4% rate of opioid misuse can be also considered an "adverse event." All prescription medications are associated with some level of risk of adverse events, and the FDA remit is in large part to balance the tradeoffs associated with treatment effectiveness and adverse events.[114] However, this balancing typically results in average rates of prescription drug adverse events between 5-10%.[115] Thus, one could consider opioid adverse event rates of 4% as being considered "actuarially expected."

5.6. The second branch of Figure 5-1 depicts the relationship between non-medical use of opioids and the potential attributable costs. Non-medical use can lead to three possible outcomes: (1) "non-cost-incurring" misuse;[116] (2) "non-cost-incurring" OUD;[117] and (3)

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[112] T. D. Saha et al., "Nonmedical Prescription Opioid Use and DSM-5 Nonmedical Prescription Opioid Use Disorder in the United States," *J Clin Psychiatry* 77, no. 6 (2016).

[113] Walley et al., "The Contribution of Prescribed and Illicit Opioids to Fatal Overdoses in Massachusetts, 2013-2015."

[114] An example of this is the management of adverse bleeding events in use of anti-thrombotic therapy. See generally K. Sugano, "How do we manage serious gastrointestinal adverse events associated with anti-thrombotic therapy?," *Expert Rev Gastroenterol Hepatol* 9, no. 1 (2015). Cardiovascular adverse events are also relatively prevalent; see for example D. M. Rackham et al., "Evidence behind FDA alerts for drugs with adverse cardiovascular effects: implications for clinical practice," *Pharmacotherapy* 34, no. 4 (2014).

[115] See generally S. V. Taché, A. Sönnichsen, and D. M. Ashcroft, "Prevalence of adverse drug events in ambulatory care: a systematic review," *Ann Pharmacother* 45, no. 7-8 (2011). Also see generally N. Rafter et al., "Adverse events in healthcare: learning from mistakes," *Qjm* 108, no. 4 (2015); R. Schwendimann et al., "The occurrence, types, consequences and preventability of in-hospital adverse events - a scoping review," *BMC Health Serv Res* 18, no. 1 (2018).

[116] An example of non-cost-incurring misuse would be taking more than the prescribed amount (for example, taking 4 pills per day instead a prescribed 3 pills per day). See generally Tetrault and Butner, "Non-Medical Prescription Opioid Use and Prescription Opioid Use Disorder: A Review."

[117] An example of non-cost incurring OUD would be an individual who experiences a delimited episode of OUD but does not seek medical attention during the episode, whose life is otherwise not meaningfully impacted by the OUD episode, and for whom there is clinical uncertainty as to differential diagnosis. See generally P. J. Freda, J. H. Moore, and H. R. Kranzler, "The phenomics and genetics of addictive and affective comorbidity in opioid use disorder," *Drug Alcohol Depend* 221 (2021); J. Strang et al., "Opioid use disorder," *Nat Rev Dis Primers* 6, no. 1 (2020); F. Vorspan et al., "Biomarkers to predict staging and treatment response in opioid dependence: A narrative review," *Drug Dev Res* 82, no. 5 (2021).

"cost-incurring" OUD.[118] These categories would also align with attributable costs, with non-cost-incurring misuse expected to have zero or negligible costs, non-cost-incurring OUD expected to have trivial or low costs, and cost-incurring OUD expected to have some measurable level of attributable costs. Based on NSDUH data, the prevalence of OUD is 0.89%, and this would apply to both OUD boxes in the diagram.[119] That leaves approximately 3% prevalence for non-cost-incurring misuse.

5.7. Returning to the discussion of the economics of externalities in Section 3, recall that four analytic tasks were identified. The discussion thus far has focused on the first two tasks: (1) documentation that a negative externality has resulted in a measurable cost that is "external" to the transaction; and (2) the identification of parties responsible for the "production" of the negative externality. The remaining tasks are (3) a calculation of the costs associated with the abatement of the externality; and (4) a mechanism by which to allocate liability (and associated abatement costs) among responsible parties. In terms of costs, I have identified in this section the pathways (and relationship, to the extent that it exists) between opioid supply and opioid costs. The final two steps—calculating the attributable costs of OUD and a mechanism by which to allocate those costs among PRPs—is beyond the scope of this report.

6. IMPLICATIONS

6.1. The preceding discussion of contributing factors, negative externalities, PRPs and OUD-attributable costs has important implications for opioid litigation generally and Montgomery County specifically. To summarize the general implications, they are as follows: (1) the drivers of opioid supply in the U.S. are multifactorial; seven factors have consistently been shown to be contributing factors in the supply of prescription opioids; (2) in economics, OUD-attributable costs can be considered negative externalities, the remedies for which require the identification of responsible parties and the allocation of responsibility among those parties; (3) the extensive literature on opioid supply clearly points to 13 different responsible parties, some of which are entities operated by the plaintiffs in these matters; and (4) the "production" of the supply of opioids is *not* the cause of the negative externality; there are two additional pathways between production and potential cost, leaving a maximum of less than 0.89% of the population "at risk" for cost-incurring OUD. Each of these general implications is also applicable to Montgomery County, in several ways.

6.2. *Nationwide Factors*. The state of Ohio and Montgomery County are subject to all factors that affect the entire country, including regulatory approval and its associated PRPs (i.e., FDA, DEA, and CDC), national trends in medical need (e.g., shift to outpatient treatment)

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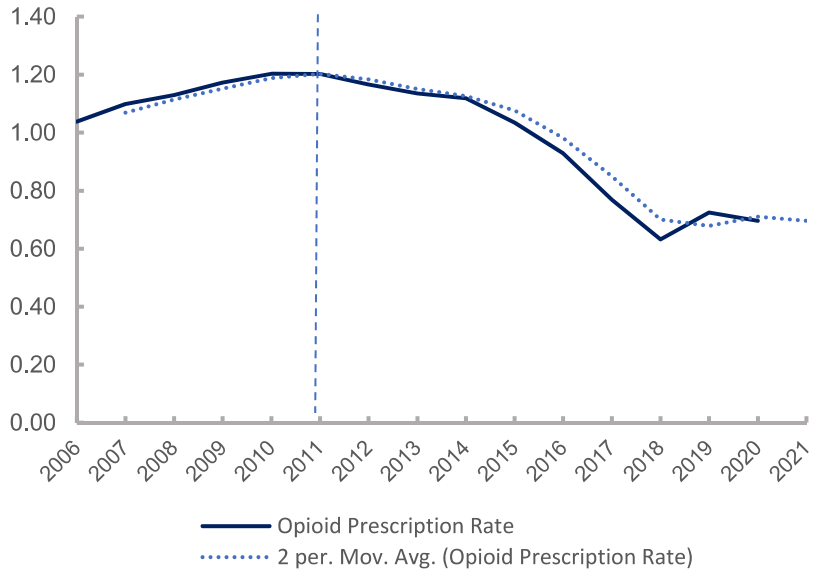
[118] An example of cost-incurring OUD would be an episode of OUD incurring medical expenses, criminal justice system expenses, and/or social and family assistance costs. See generally Davenport, Weaver, and Caverly, "Economic Impact of Non-Medical Opioid Use in the United States: Annual Estimates and Projections for 2015 through 2019."

[119] In the diagram, the 0.89% OUD prevalence must be split between the two OUD boxes; thus, I depict each OUD box as having < 0.89% prevalence, which suggests some unknown split between the two boxes.

quality ratings and its associated PRPs (e.g., Joint Commission; national payers like Medicare and large commercial payers), pain management advocacy on the part of federal government agencies, pain management advocacy on the part of national medical societies, national manufacturer marketing, and national macroeconomic factors.[120]

6.3. Montgomery County's rate of prescription opioids also aligns with national trends. Figure 6-1 shows opioid prescriptions per capita, based on CDC data on opioid prescriptions by state and county.[121] As the figure shows, the opioid prescription rate per 100,000 declined substantially from about 2011 onwards, appearing to level off to some degree around 2018[122]—a trend largely consistent with national trends. This fall in prescription opioid rates has been described elsewhere; for example, Bowman reports that in Montgomery County the "presence of prescription opioids" decreased substantially from 74% in 2010 to 18% in 2016.[123]

Figure 6-1. Opioid Prescription Rate Per 100,000 Population: Montgomery County, 2006-2021



6.4. *Medical Need*. Montgomery County has higher levels of comorbidities compared to the rest of Ohio and the U.S. According to a 2021 report from the Ohio Department of Health, in Montgomery County,[124] 22.1% of adults are current smokers, compared with 21.4% in Ohio and 17% in the U.S.; 35.6% of adults are obese, compared with 33.5% in Ohio and 30% in the U.S.; 27.0% of adults are physically inactive, compared with 26.1% in Ohio and 23% in the U.S. In addition, the incidence of any cancer (2014-2018) was 471.5 per

[120] See generally L. Leduc, "Solving the Opioid Epidemic in Ohio," *J Law Health* 32, no. 1 (2019).
[121] CDC, "Opioid Precribing Data, 2006-2020."
[122] The leveling of the rate is more noticeable in the dashed line, with is the two-year moving average.
[123] M. Bowman, "Opioid Abuse and Death: Thoughts From Dayton, Ohio," *Fam Med* 50, no. 6 (2018).
[124] ODH, "Montgomery County Cancer Profile," (Columbus, OH: Ohio Department of Health, 2021).

100,000 residents, compared to 467.5 per 100,000 in Ohio and 450.5 per 100,000 in the U.S. Based on these data, it is reasonable to expect a generally higher level of need in Montgomery County versus the rest of the state and the U.S.

6.5. *Physicians*. Montgomery County has been home to some of the larger profile cases of "pill mills" run by physicians. There are several examples that resulted in criminal prosecution, including a Dayton-area physician who distributed nearly 4,000 units of oxycodone "outside the scope of medical practice" and "not for a legitimate medical purpose."[125] Another case involved a physician sentenced to three years in prison for "running two 'pill mills' in Dayton and New Carlisle."[126]

6.6. *Government*. In the first physician example above, all the opioid units distributed in that Montgomery "pill mill" were paid for by Medicare or Ohio Medicaid.[127] As I discussed above, both entities would have had the ability to leverage their detailed claims data to identify at-risk patterns and intervene in the physician's practice. In addition, Montgomery County self-insures its employees, and could have used its own healthcare administrative data to detect irregular patterns and take corrective actions.

6.7. *Quality Ratings*. In addition to the influences of nationwide entities tying accreditation and reimbursement to quality ratings and pain management scores, the state of Ohio has separately contributed to these influences through its own Medicaid program. For example, the provider contract for Ohio Medicaid Managed Care describes its reliance on HEDIS quality measures, including patient satisfaction.[128] In addition, Montgomery County is self-insured and contracts with Anthem Blue Cross Blue Shield ("Anthem") to administer health insurance benefits to its employees.[129] Anthem widely publicizes its reliance on HEDIS metrics in provider contracting.[130]

6.8. *Manufacturers & Distributors*. Manufacturer marketing has been an issue in Ohio and Montgomery County.[131] The Ohio Attorney General has already reached settlements with pharmaceutical manufacturers Endo and Johnson & Johnson,[132] and has also reached settlements with independent distributors McKesson, Amerisource-Bergen, and Cardinal Health.[133]

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[125] B. McNeal, "Dayton doctor sentenced for running pill mill," news release, 2019.
[126] OAG, "Attorney General DeWine Announces Dayton-Area Pill Mill Doctor Sentenced to Three Years in Prison," news release, 2012.
[127] McNeal, "Dayton doctor sentenced for running pill mill."
[128] ODM, "Ohio Department of Medicaid Ohio Medicaid Provider Agreement for Managed Care Organizations," (Ohio Department of Medicaid, 2021).
[129] See http://www.mcbenefits.org/docs/Benefits_Booklet_2022.pdf.
[130] See, for example, Anthem, "HEDIS 101 for providers, 2019: Improving quality of care," (Anthem Blue Cross and Blue Shield, 2019).
[131] Leduc, "Solving the Opioid Epidemic in Ohio."
[132] C. Minhee, "Opioid Settlement Tracker," (2022).
[133] OAG, "AG Yost Announces Ohio's Historic $808 Million Settlement with Opioid Distributors," news release, 2021.

6.9. *Macroeconomic Factors*. Montgomery County saw steadily increasing unemployment rates from the mid-1990s through 2010,[134] which aligned with an increase in OUD rates over the same period. Montgomery County's unemployment rate reached a high of 13.2% in 2010, 4 percentage points higher than the 9.3% U.S. rate in the same year.

6.10. *Drug Trafficking*. Montgomery County qualifies as one of 33 HIDTAs nationally, meaning that it is known to be at elevated risk for significant intrusion of illicit drugs, including opioids. Across Ohio, the amount of heroin seized by law enforcement increased by about 1,200% in a single year from 2009 to 2010.[135] As discussed in Section 4, in the Ohio HIDTAs, the U.S. DOJ reported that heroin availability increased in the Ohio HIDTA region because of an increased supply of Mexican heroin, "leading law enforcement agencies to identify heroin as the greatest drug threat in the region." The influx of illicit opioids is clearly having an upward effect of OUD rates in Montgomery County. The capacity of the United States, the state of Ohio, and Montgomery County to eliminate or even substantially reduce illicit drug supply from abroad is limited.

7. COMMENT ON CUTLER REPORT

7.1. *General Comments.* Overall, I disagree with Cutler's opinions and findings, for several reasons. To summarize, the main flaws and limitations of Cutler's report are as follows: (1) the analysis fails to recognize or account for all the various supply-side and demand-side contributing factors associated with the supply of prescription opioids, which I described in detail above; (2) the analysis fails to make a connection between the operations of retail pharmacies and the volume of prescription opioids; a direct relationship is assumed, but the logic of the relationship is nonexistent and contradictory; (3) the logic of the relationship between the operations of retail pharmacies and the prevalence of OUD and the magnitude of OUD-related mortality is nonexistent; (4) Cutler fails to recognize that all of the behavior that plaintiffs attribute to retail pharmacies related to "what should have been done" could very easily be attributed to a long list of other entities, including the plaintiffs themselves; and (5) regression analysis is put forward as the primary evidentiary support of these relationships, but the regressions exhibit a number of flaws that drastically limit the relevancy and accuracy of the findings. The following sections provide some additional detail on these findings.

7.2. *Causal Pathways*. Another general comment is that Cutler implies a causal pathway of this sort: Retail Pharmacies → Opioid Supply (or "shipments") → Opioid Misuse → OUD Attributable Costs. This causal link is critical to eventually arriving at his main opinion, which is that retail pharmacies (via opioid shipments) "cause" OUD attributable harms and costs. However, the evidence he puts forward for each of these links in the causal chain is either non-existent or weak, including his own regression analyses.

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[134] U.S. Bureau of Labor Statistics, Unemployment Rate in Montgomery County, OH, retrieved from FRED, Federal Reserve Bank of St. Louis; https://fred.stlouisfed.org/series/OHMONT3URN.
[135] USDOJ, "Ohio High Intensity Drug Trafficking Area."9.3

7.3. First and foremost, there is no logical or evidentiary basis as to how retail pharmacies can create or induce "sales" of prescription drugs. Community-based and hospital-based physicians are the only source of opioid prescriptions. A retail pharmacy cannot dispense a filled prescription without a verified and legal prescription initiated by a licensed healthcare provider. Moreover, as discussed above in my report, shipments of opioids cannot legally exceed quotas established by the DEA.

7.4. Second, Cutler fails to provide sufficient logic and evidence on the causal connection between prescription opioid supply and opioid misuse, for the following reasons: (1) as the volume of prescription opioids has declined, over the past decade an increasing proportion of misuse is driven by illicit opioids, the supply of which has increased over the same decade. and (2), as discussed in more detail below in the context of Cutler's regression models, the hypothesis that the supply of prescription opioids drives misuse suffers from "omitted variable bias" and "endogeneity;" omitted variable bias because there are many well-documented drivers of misuse that are excluded from Cutler's analysis, and endogeneity because opioid misuse is likely to some degree endogenous to opioid supply.

7.5. Third, Cutler fails to provide sufficient logic and evidence on the causal connection between prescription opioid supply and OUD, for the following reasons: (1) given that, according to NSDUH, the prevalence of opioid misuse in the U.S. is about 3.59%, and the prevalence of OUD is 0.89%, the implication (based on these data alone) are that less than 25% of those who misuse opioids progress to OUD;[136] (2) differentiation (via toxicology) between prescription and illicit sources in OUD cases are performed in less than 50% of cases, which implies that there are high levels of uncertainly as to the opioid sources in OUD cases;[137] (3) at least 60% of OUD cases are attributable to illicit opioids,[138] and the rate of illicit opioid use has been rising.[139]

7.6. *Role of Retail Pharmacies*. Cutler opines that "*...defendants have strong economic incentives to increase sales of prescription drugs, including opioids* (emphasis added).[140] The main problem with this argument is that retail pharmacies are not able to "increase sales of prescription drugs." Retail pharmacies are legally bound to only dispense prescriptions to customers with valid, verified prescriptions from physicians. There are

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[136] Given the inaccuracies in the data on differentiating between OUD attributable to prescription opioids and OUD attributable to illicit opioids (e.g., due to inconsistencies in toxicology testing, etc.), it is likely that the population prevalence of OUD attributable to prescription drugs is considerably lower than 0.89%. (Also see OIG, "Review of the Drug Enforcement Administration's Regulatory and Enforcement Efforts to Control the Diversion of Opioids.") Thus, based NSDUH data, the proportion of misuse that progresses to OUD is likely to be considerably less than 25%.

[137] D.R. Little et al., "Only 5% of Overdose Patients Tested for Fentanyl, #1 Killer of Americans 18-45," (Verona, WI: Epic Research, Epic Systems Corporation, 2022).

[138] For example, see Walley et al., "The Contribution of Prescribed and Illicit Opioids to Fatal Overdoses in Massachusetts, 2013-2015."

[139] D. Ciccarone, "The rise of illicit fentanyls, stimulants and the fourth wave of the opioid overdose crisis," *Curr Opin Psychiatry* 34, no. 4 (2021); GAO, "Illicit Opioids: While Greater Attention Given to Combating Synthetic Opioids, Agencies Need to Better Assess their Efforts."

[140] Cutler, ¶ 29

not practical or legal means by which retail pharmacies could "induce" demand for any prescription drug, including opioids. Advertising and discounts on specific prescription drugs, for example, are solely for the purpose of competition for market share between retail pharmacy chains, not to "induce" the creation of new prescriptions.

7.7. Later Cutler states that "Defendants thus face an economic decision about how to balance the competing incentives of (i) incurring costs to comply with legal obligations to identify and deny fulfillment of prescriptions unrelated to medical need and at risk of diversion; and (ii) loss of revenue and profit associated with restricting opioid sales."[141] This raises two important points. First, Cutler departs from the perplexing argument that retail pharmacies can induce demand for prescriptions, and directly implies here that the role of retail pharmacies is exclusively in the realm of "demand control," (e.g., monitoring) and not creation of opioid supply or "supply-push." In other words, he opines that retail pharmacies can only address opioid utilization on the demand side by disentangling appropriate demand from inappropriate demand.

7.8. Plaintiffs (and Cutler) make the argument that the cause of problems stemming from opioids is largely due to the volume of shipments and dispensed prescription opioids. Indeed, that appears to be the main premise of Cutler's report, and he emphasizes that again in the discussion around Exhibit 6. However, there are three very important observations regarding this upward sloping curve shown in the Exhibit: (1) the slope of the curve can logically only be a function of factors that are able to *create* supply ("supply-push") and *create* demand ("demand pull"), yet Cutler seems to admit at times that retail pharmacies can do neither of these; (2) even if one were adopt the non-sensical position that retail pharmacies can in fact create supply and demand for opioids, there are a host of other factors that have been proven to have done the same; and (3) Cutler makes no direct causal connection between the operations of retail pharmacies and OUD; the causal link remains purely speculative, and Cutler's regression analyses (discussed below) do not solve that problem.

7.9. *Responsible Parties*. Again, Cutler suggests that the volume of prescription opioids is solely the responsibility of "Manufacturers, distributors, and dispensers [i.e., retail pharmacies]," which is how he depicts it in Exhibit 5. As my discussion above suggests, this is clearly incorrect, and in his deposition transcript he seemed also doubt the accuracy of his own diagram.[142] There is a robust body of evidence identifying a relatively long list of factors that have contributed to the supply of opioid prescriptions, as I have discussed in detail above. Most of these factors work through the common channel of medical care providers initiating or continuing treatment, though Cutler appears to ignore the important role of physicians and hospitals and their sole control on the issuing of opioid prescriptions. Again, retail pharmacies cannot dispense prescription opioids to consumers without first receiving legal prescriptions written by practicing physicians.

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[141] Cutler, ¶ 30

[142] For example, on page 73 (lines 3-8), Cutler is asked "and other actors could have contributed to the supply of opioids beyond just the three that you have identified. Correct?" To which he answers "That is correct, yes. In fact, the literature has many other actors that it blames as well."

7.10. Perhaps more importantly, Cutler fails to recognize or account for the fact that many other entities could similarly have played a part in detecting inappropriate prescriptions, including the plaintiffs themselves. In fact, Cutler would agree that the following entities possess more expansive and complete data than retail pharmacies and would have been able to detect opioid-related prescribing issues *before* and more *effectively* than retail pharmacies: (1) federal Medicare program; (2) Ohio Medicaid program; (3) private insurers; (4) the state of Ohio, in its role as a self-insured employer; (5) Montgomery County government, in its role as a self-insured employer; (6) Ohio state government and Montgomery County government, via the Alcohol, Drug Abuse, and Mental Health Services ("ADAMHS") tracking system; (7) the State Medical Board of Ohio ("SMBO");[143] (8) the DEA, in its role establishing quotas and monitoring shipments of Schedule I and II prescription drugs; and (9) the CDC, in its role as the nation's lead agency responsible for monitoring and managing of health issues.

7.11. Cutler also is of the opinion that opioids shipped to Montgomery County did not reflect "medical need." I disagree. First, as I noted above, the Montgomery County population is "less healthy" than the population of Ohio and the U.S. in four key health metrics. Second, there is general agreement that some proportion of opioid prescribing nationally did not reflect medical need, and instead reflected the need for effective pain management after surgery; for example, a study evaluating post-discharge opioid prescribing and use after common surgical procedures found that 76% of patients received an opioid prescription after surgery.[144] Opioid shipments reflect opioid *prescriptions*, and some percentage of opioid prescriptions written by physicians were believed to have been inappropriate or unnecessary. Questioning the medical necessity of a treatment, regardless of whether it is a pharmacological treatment, surgical treatment, or other type of treatment, is only within the scope of practice of licensed physicians.

7.12. *Effect on OUD*. Cutler offers the opinion that prescription opioids are the main driver of OUD and OUD mortality. Despite the rapid decline in opioid prescription rates in the U.S. and in Montgomery County in recent years (as I show above), alongside a dramatic increase in the utilization of illicit opioids, plaintiffs argue that it is the high rates of prescription opioids from past decades that is driving the demand for illicit opioids. There are four limitations to this argument: (1) attributing OUD to prescription opioids (putting aside for a moment the aforementioned problems with that) is *not* equivalent to attributing OUD to retail pharmacies; (2) there are many factors driving prescription opioid supply, as discussed above in my report; (3) the evidence that illicit opioid abuse is in some way "due to" early abuse of prescription opioids is not well established; and (4) it is possible that some illicit opioid abuse is preceded by abuse of *diverted* prescription opioids, but the

[143] According to its mission statement, "The State Medical Board of Ohio ["SMBO"] issues licenses and *oversees the practice* of allopathic physicians (MD), osteopathic physicians (DO), podiatric physicians (DPM), massage therapists (LMT), and cosmetic therapists (CT) under the authority of the Medical Practices Act, Chapter 4731, Ohio Revised Code (ORC)" (emphasis added). It summarizes its mission as follows: "To protect and enhance the health and safety of the public through effective medical regulation."
[144] M. H. Fujii et al., "Post-Discharge Opioid Prescribing and Use after Common Surgical Procedure," *J Am Coll Surg* 226, no. 6 (2018).

association between retail pharmacy operations and post-dispensing diversion is not established.

7.13. *Regression Analysis*. Cutler puts forth a series of regression analyses to determine whether (or the extent to which) opioid shipments "caused" OUD and OUD mortality, forming the primary evidentiary base for his opinions regarding liability. He states that "Establishing a causal relationship requires demonstrating that the 'effect' was not the result of other factors that are not properly accounted for in the analysis."[145] While this statement above is generally correct, there are several serious flaws to this approach, and these flaws severely limit the interpretability and relevance of his regression findings. Though there are several methodological flaws with the regressions, three stand out as very important. These three problems greatly limit the interpretability of Cutler's regressions.

7.14. First, the regressions are missing the entire "front end" necessary to link alleged behavior of retail pharmacies with volume of prescription opioids. In other words, without connecting pharmacy operations and the volume of opioid prescriptions, there is no way to interpret the role of shipments in the regression equation. Again, this is a problem throughout his report, where he depends very heavily on the non-sensical notion that retail pharmacies are somehow able to (1) induce demand for additional prescription sales, or (2) induce community physicians to write more opioid prescriptions.

7.15. Second, the regressions suffer from "omitted variable" bias[146] in that right-hand side variables (i.e., the independent "explanatory" variables) do not include most the factors that can lead to OUD and OUD-related mortality. This is of particular importance in models of causality; for example, Vittinghoff et al., a commonly used graduate text for regression methods in biostatistics, states that, "The assumption of no unmeasured confounders is common to most causal modeling methods and is crucial to achieving conditional independence of exposure from potential outcomes."[147] In regression analysis, omitted variable bias limits the interpretability of the coefficients and *t*-statistics. This is because the included variables are left to explain more of the variation in the dependent variable, even if the role of included variables is relatively small or unimportant. In Cutler's regressions, there are many omitted variables, including patient characteristics, patient comorbidities, the role of illicit opioids, treatment modalities, and the role of co-occurring SUD, each of which would be expected to be included in a mortality or survival model.[148] In addition, Cutler's regression models contain very few "supply side" variables,

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[145] Cutler, ¶ 107

[146] See generally R. Xu, "Statistical methods for the estimation of contagion effects in human disease and health networks," *Comput Struct Biotechnol J* 18 (2020); P. Kennedy, *A Guide to Econometrics (Fourth Edition)* (Cambridge, MA: MIT Press, 1998).

[147] See Chapter 9 of E. Vittinghoff et al., *Regression Methods in Biostatistics (Second Edition)*, ed. M. Gail and et al., Statistics for Biology and Health (New York, NY: Springer Science and Business Media, 2012).

[148] See generally M. J. Bradburn et al., "Survival analysis Part III: multivariate data analysis -- choosing a model and assessing its adequacy and fit," *Br J Cancer* 89, no. 4 (2003); M. Pavlou et al., "Review and evaluation of penalised regression methods for risk prediction in low-dimensional data with few events," *Stat Med* 35, no. 7 (2016); D.W. Hosmer, S. Lemeshow, and S. May, *Applied Survival Analysis (Second*

as I described above. In the presence of high levels of omitted variable bias, it is impossible to interpret the coefficient on opioid shipments as anything other than a correlation.

7.16. Third, Cutler's regressions are likely to suffer from endogeneity, which occurs when an independent variable is correlated with the error term in the model. Specifically, in Cutler's model, he is hypothesizing that opioid supply "causes" OUD (i.e., "supply push"), but if this is the case than it could also be the case that OUD "causes" opioid supply (i.e., "demand pull"). An example of the latter would be patient drug-seeking behavior on the part of individual with OUD. This is also referred to as "simultaneity." Like omitted variable bias, the presence of endogeneity is likely to bias the regression results.[149] There are common techniques to address this problem, such as two-stage least squares regression ("2SLS"), but Cutler does not appear to even recognize the problem.

7.17. To further explore the likely endogeneity problem, I replicated Cutler's regressions using instrumental variables ("IV") with 2SLS. Cutler's cancer mortality rate variable was selected as the instrument due to a moderate correlation with the opioid shipments variable (coefficient = 0.3579), as well as a qualitative linkage (i.e., via "demand pull"). I specified a first-stage regression of shipments as a function of cancer rates, and then included the predicted value in the second-stage regression (i.e., Cutler's original regression, less the cancer rate variable). This did not affect the overall performance of the model substantially; R-squared values of the first stage linear regression were comparable to the original Cutler regressions. In the second-stage models, the opioid shipments variable was no longer statistically significant (i.e., not statistically different from zero), and the second-stage regressions had markedly lower R-squared values compared to Cutler's reported regressions. The fact that the statistical significance of Cutler's main variable of interest (opioid shipments) becomes "zero" in models appropriately adjusting for endogeneity suggests that endogeneity is indeed a serious problem in Cutler's regressions.

8. COMMENT ON ALEXANDER REPORT

8.1. *General Comment*. In this section I provide some comments on the expert report submitted by Caleb Alexander in the Montgomery County matter. I begin with the general comment that Alexander's main goal in his report is to identify any public service that could plausibly be impacted by OUD. The implications are that for each of these services, one could readily identify a share of the Montgomery County operational costs that can be attributable to OUD and, presumably, further attributable to the supply of prescription opioids. I disagree with this basic premise. Some proportion of SUD-attributable externality costs (e.g., alcohol, tobacco, or illicit drugs) are "actuarily expected" and factored into the budgets of all states, counties, and municipalities. Repurposing some proportion of existing assets to OUD, even if we were to be able to accurately determine that proportion, does not necessarily constitute an attributable cost. This is especially

Edition), ed. D.J. Balding and et al., Wiley Series in Probability and Statistics (Hoboken, NJ: Wiley-Interscience, 2008).

[149] Refer to Kennedy, *A Guide to Econometrics (Fourth Edition)*; G. Zaefarian et al., "Endogeneity bias in marketing research: Problem, causes and remedies," *Industrial Marketing Management* 65 (2017).

relevant in the presence of high fixed costs, which is an issue that I discuss in greater detail below.

8.2. *Abatement*. Alexander's report focuses mainly on abatement;[150] specifically, Montgomery County services and departments in which OUD attributable abatement costs are "expected" to be incurred. He does not calculate or imply a specific abatement amount, but instead adopts a "kitchen sink" approach to listing all conceivable cost centers potentially associated with OUD. However, this raises two important general comments: (1) the listed services are applicable to all types of SUD and related services, and difficult to disentangle from OUD-related cases; and (2) services that have been and continue to be part of the County's normal and routine service offerings (i.e., wherein fixed costs represent a large proportion of total costs). Alexander does not provide any evidence that the activities of these public services incurred additional costs specifically attributable to OUD. Moreover, these public services do not distinguish or reliably record whether an incurred cost was attributable to prescription opioids versus illicit opioids. For example, a study based on electronic medical records found that toxicology to determine opioid source was only performed in only 50% of overdose cases treated in hospital EDs, and fentanyl tests were performed in only 5% of cases.[151]

8.3. In his discussion of various services that could plausibly manage OUD cases, Alexander ignores the crucial role of fixed versus variable costs. There is a percentage of public costs that are fixed, and do not vary with the volume of services provided. By most accounts, in public services at least 50% of costs do not vary in the short run.[152] So, even if one were to assume that some proportion of public expenditures is indeed attributable to OUD (more specifically, OUD associated only with prescription opioids), there is still the question of what percentage of those costs are fixed and unlikely to vary with the volume of services. Allocating attributable externality costs to fixed costs requires a different approach compared to variable costs.

8.3.1. In the criminal justice system ("CJS") context, Wilson and Lemoine conducted a comprehensive literature review of the role of marginal, variable, and fixed costs in the corrections sector of CJS.[153] The authors focus on "marginal costs," which is a very common concept in the field of economics. Marginal cost refers to the additional costs needed to produce one more unit of output. In the case of police, it would be, for example, the added costs associated with one additional arrest (or preventative effort). In the instance of courts, it would be the costs associated with one additional court case. In the example of prisons, it would be the costs associated with the housing of one additional inmate. It follows that marginal costs pertain primarily to variable

[150] Although it was my understanding that reports filed at this time are intended to focus on liability, there are 83 occurrences of the word "abatement" in Alexander's report.
[151] Little et al., "Only 5% of Overdose Patients Tested for Fentanyl, #1 Killer of Americans 18-45."
[152] See, for example, C. Henrichson and S. Galgano, "A Guide to Calculating Justice-System Marginal Costs," (Washington, D.C.: U.S. Department of Justice: Bureau of Justice Assistance, 2013); S.J. Wilson and J. Lemoine, "Methods of Calculating the Marginal Cost of Incarceration: A Scoping Review," *Criminal Justice Policy Review* (2021).
[153] "Methods of Calculating the Marginal Cost of Incarceration: A Scoping Review."

costs, which can be changed in the short run, and less to fixed costs, which do not change in the short run and are not sensitive to "marginal" changes in output. The authors found that in the short run, about 80% of average costs are fixed; that is, these costs do not change with fluctuations in the number of individuals entering the CJS. In the longer run, however, this amount falls to about 30%.

8.3.2. In economics, the concepts of short-run and long-run do not necessarily pertain to specific lengths of time, as the length of time would vary considerably by industry and by the ratio of fixed versus variable costs required to operate (as in this case).[154] In the case of CJS and social and family assistance ("SFA"), if 80% of costs are fixed in the short run and 30% are fixed in the long run, it is reasonable to assume that, for some arbitrarily "moderate" length of time, about 50% of costs would be fixed. Thus, I assume that only 50% of CJS and SFA costs are fixed (i.e., and not influenced by OUD-related issues). I believe that this is a conservative estimate, and that it could be argued that a higher proportion of costs (60%-70%) remains fixed for a relatively long period of time, given the nature of operations characterized by high fixed costs and rigid tax-based budgets determined several years prior. For example, a study by the U.S. Department of Justice found that prison costs are 86% fixed in the short run and 56% fixed in the long run, the average of which is 71% fixed costs.[155]

8.3.3. This concept is very important to OUD-attributable costs and abatement because a large proportion of the average costs (i.e., total operating divided by total quantity of output) for police, courts, corrections, and social assistance are expected to be fixed in the short run. This is compounded by the fact that these types of budgets are publicly funded from general tax revenue and determined far in advance of when they are utilized. In the short run, states and municipalities cannot easily add physical capacity (e.g., expanded or additional buildings, police stations, court houses, and prisons); likewise, with budgets being relatively fixed in the short run, state and local governments are limited even in their ability to add variable costs (e.g., personnel; supplies).

8.4. Regarding abatement, Alexander implies that his lengthy list of public services would constitute items included in abatement, and further suggests that these costs have already been incurred. Yet he also makes the point that many of the initiatives already in place to reduce opioid supply have already succeeded in doing so, and this in turn has created more demand for illicit opioids. If we are to assume that is true, then the costs associated with "initiative-related demand" should be "deductible" from OUD-attributable abatement costs. In other words, insofar as pharmacies have done their part in further limiting supply of prescription opioids, then they cannot then also be held liable for the subsequent increasing demand for illicit opioids. This is an important point, as the majority of OUD going forward is attributable to illicit opioids. Alexander suggests that many of the Montgomery County services and departments he identifies have already been engaged in OUD-related activities and are to some extent "affected by" OUD-attributable costs.

[154] See generally Nicholson and Snyder, *Microeconomic Theory: Basic Principles and Extensions, 12th Edition*.

[155] Henrichson and Galgano, "A Guide to Calculating Justice-System Marginal Costs."

However, Alexander fails to identify the pathways and mechanisms through which such potential abatement costs are expected to be incurred.

8.5. This is a county-level matter, yet Alexander provides no discussion or analysis as to how services are differentially financed at the federal, state, county, and municipality levels. For most of the services that Alexander identifies, there is significant cost sharing with either the state or federal government. This is a very important consideration regarding abatement, as such cost-sharing arrangements are especially common among social services.[156] For healthcare costs, the Centers for Medicare and Medicaid Services ("CMS") administers the Medicaid program as a "co-funded" program, whereby approximately 30-50% of incurred costs are paid by state Medicaid programs and approximately 50-70% are paid by the Federal government.[157] The exact split varies by state; for example, in Ohio, the Federal government funds 64% of the Medicaid program and the state of Ohio funds the remaining 36%.[158] Note that the Federal government does not act as an "insurer" in this capacity; rather, the total budget is shared between the two entities to co-fund the program. Similar cost sharing arrangements exist for SFA. In general, the federal government funds 65% of all public welfare expenditures, mainly through federal intergovernmental grants to state and local governments.[159] This general split appears to be applicable to Ohio, which for example received 64.3% of its $1.3 billion TANF[160] funding via federal block grants in 2018.[161]

8.6. Many of the services Alexander deems essential for abating the alleged costs of OUD represent activities that could have been employed by the plaintiffs to potentially identify OUD earlier. This is a point I have made in several places in my report. For example, the state Medicaid program, state and local law enforcement, state and local courts, and state and local social and family assistance programs were all well-positioned to play some role in the detection and prevention of OUD-attributable harms or costs.[162] In addition, Montgomery County is self-insured, and the data available to the county via that arrangement would have been more than sufficient to identify potential problems among the more than 1,000 county employees.

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[156] See generally R.D. Lee, R.W. Johnson, and P.G. Joyce, *Public Budgeting Systems (10th Edition)* (Burlington, MA: Jones & Bartlett Learning, 2021).

[157] See generally Commonwealth Fund, "What Is Medicaid's Value?," (New York, NY 2019).

[158] KFF, "Medicaid in Ohio," (Washinton, D.C.: Kaiser Family Foundation, 2022).

[159] Urban Institute, "Public Welfare Expenditures," in *State and Local Backgrounders* (Washington, DC: The Urban Institute, 2022).

[160] TANF refers to the state-administered "Temporary Assistance for Needy Families."

[161] W. Patton, "Ohio Budget Basics: 2019 Budget Primer," (Cleveland, OH: Policy Matters Ohio, 2019).

[162] See generally J. A. Arruda, N. A. Kurtzman, and V. K. Pillay, "Prevalence of renal disease in asymptomatic heroin addicts," *Arch Intern Med* 135, no. 4 (1975); W. Gao et al., "Predicting opioid use disorder and associated risk factors in a Medicaid managed care population," *Am J Manag Care* 27, no. 4 (2021); B. Saloner et al., "Predictive Modeling of Opioid Overdose Using Linked Statewide Medical and Criminal Justice Data," *JAMA Psychiatry* 77, no. 11 (2020); G. A. Subramaniam and M. A. Stitzer, "Clinical characteristics of treatment-seeking prescription opioid vs. heroin-using adolescents with opioid use disorder," *Drug Alcohol Depend* 101, no. 1-2 (2009); J. Tong et al., "Identifying Clinical Risk Factors for Opioid Use Disorder using a Distributed Algorithm to Combine Real-World Data from a Large Clinical Data Research Network," *AMIA Annu Symp Proc* 2020 (2020).

8.7. Alexander implies that "full abatement" of OUD should be the goal. Yet, as experts in the field of public health understand well, in the U.S. there are levels of externalities, including pollution, contamination, and attributable illnesses and conditions, that are "actuarily expected" and "implicitly accepted." In other words, as a society we implicitly "accept" some amount of air pollution, some amount of soil contamination, some amount of crime, and some number of annual deaths from smoking (480,000 per year), alcohol (140,000 per year), and motor vehicle accidents (43,000 per year).[163] For each of these externalities, there are extensive programs, laws, and policies aimed at prevention and mitigation, yet the societal goal is clearly *not* to reduce the attributable costs of these externalities to $0. Instead, the goal is to arrive at some "actuarily expected" or "implicitly accepted" rate of what could be considered adverse events associated with the activity.

9. SUMMARY

9.1. *Contributing Factors*. Contributing causative factors are those that in some way created, enabled, perpetuated, or promoted opioid sales, either in the form of supply-push or demand-pull. The following factors have been identified by experts as critical drivers of the supply of prescription opioids: (1) regulatory approval; (2) changes in medical need; (3) government advocacy for pain management; (4) medical advocacy for pain management; (5) increased reliance on "quality" ratings in accreditation and reimbursement systems; (6) manufacturer marketing to physicians; and (7) macroeconomic factors. In statistical models of causality, it is important to capture as many of the contributing factors as possible.

9.2. *Externalities*. Economists have described specific remedies and policy instruments to address negative externalities, including taxes, regulation, bargaining, and courts. Generally, the implementation of such remedies requires four primary sources of information: (1) documentation that a negative externality has resulted in a measurable harm or cost that is "external" to the transaction; (2) the identification of parties responsible for the "production" of the negative externality (e.g., in the case of carbon dioxide, it is not caused by a single factory but multiple factories, and not a single vehicle but multiple vehicles, etc.); (3) a calculation of the costs associated with the abatement of the externality; and (4) a mechanism by which to allocate liability (and associated abatement costs) among responsible parties.

9.3. *Responsible Parties*. the previously discussed contributing factors to opioid supply map to the following PRPs: (1) FDA; (2) DEA; (3) CDC; (4) Physicians; (5) Health Systems; (6) Patients; (7) Federal government; (8) State government; (9) Accreditation agencies; (10) Payers; (11) Manufacturers; (12) Distributors; and (13) Drug traffickers.

9.4. *Externality Costs*. Non-medical use of prescription opioids has a prevalence of about 4%. Non-medical use can lead to three possible externality outcomes: (1) "non-cost-incurring" misuse; (2) "non-cost-incurring" OUD; and (3) "cost-incurring" OUD. These categories

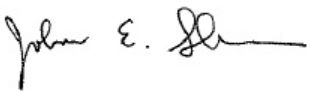
[163] Based on CDC data.

would also align with attributable costs, with non-cost-incurring misuse expected to have zero or negligible costs, non-cost-incurring OUD expected to have trivial or low costs, and cost-incurring OUD expected to have some measurable level of attributable costs. Based on NSDUH data, the prevalence of OUD is 0.89%, and this prevalence would apply cost-incurring and non-cost incurring OUD (i.e., would need to be further divided across the two groups).

9.5. *Implications*. The state of Ohio and Montgomery County are subject to all factors that affect the entire country, including regulatory approval and its associated PRPs (i.e., FDA, DEA, and CDC), national trends in medical need (e.g., shift to outpatient treatment) quality ratings and its associated PRPs (e.g., Joint Commission; national payers like Medicare and large commercial payers), pain management advocacy on the part of federal government agencies, pain management advocacy on the part of national medical societies, national manufacturer marketing, and national macroeconomic factors. Montgomery County is also less healthy, which implies that a larger proportion of opioid shipments could be explained by medical need. The county has also had to contend with some high-profile "pill mills" run by multiple area physicians. Finally, the county has experienced unemployment rates significantly higher than the nation, which likely exacerbated macroeconomic drivers of SUD.

9.6. *Plaintiff Experts*. The expert report filed by David Cutler attempts to make the case, using regression analysis, that shipments of prescription opioids "caused" OUD in Montgomery County, though he does not conclude that shipments were the sole cause. However, he fails to make an evidence-based argument that supports each of the links in the causal chain between retail pharmacies and the OUD externality. A critical underpinning of plaintiff arguments generally, and Cutler's specifically, is that retail pharmacies can somehow generate demand for new prescriptions. I disagree, as any new prescription must originate from a licensed health care provider. Cutler's regressions, which he puts forth as evidence of a causal link between opioid shipments and associated externalities, have some serious limitations that limit their applicability, but more importantly Cutler does not attempt to identify or control for all contributing factors or PRPs, leaving his regression results unhelpful in determining shares of the costs of the externality. The report filed by Alexander is flawed mainly in that he asserts that a long list of government agencies and entities have incurred (or will incur in the future) OUD-attributable costs but offers little evidence as to how the operational functions of these entities were changed by OUD (or are expected to be changed by OUD), and how OUD may have differentially impacted fixed versus variable costs.

The opinions and conclusions put forward in this report represent are all within a reasonable degree of certainty in the fields of economics, health economics, biostatistics, epidemiology, and health services research. In addition, I reserve the right to amend and revise this report as additional data and information become available.



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